Welcome!

SurfON Study

Site Initiation Visit (SIV) –Training

Delivered by Marie Hubbard (Co-Investigator) & Christina Cole – Senior Trial Manager

Presentation overview

PART I – Study Overview & Procedures

Safety Reporting & Hospital Transfers

PART II – Data Management

PART III – Study Documentation & administration

Part I - Presentation overview

STUDY OVERVIEW

- Background information
- Current practice & hypothesis
- Study objectives
- Study Design
- Primary/secondary outcomes
- Inclusion/exclusion criteria

STUDY PROCEDURES

- Study Protocol
- Screening & eligibility check
- Informed consent procedure
- Randomisation
- Surfactant administration
- Health questionnaires
- Remote follow up
- Withdrawals

SAFETY REPORTING

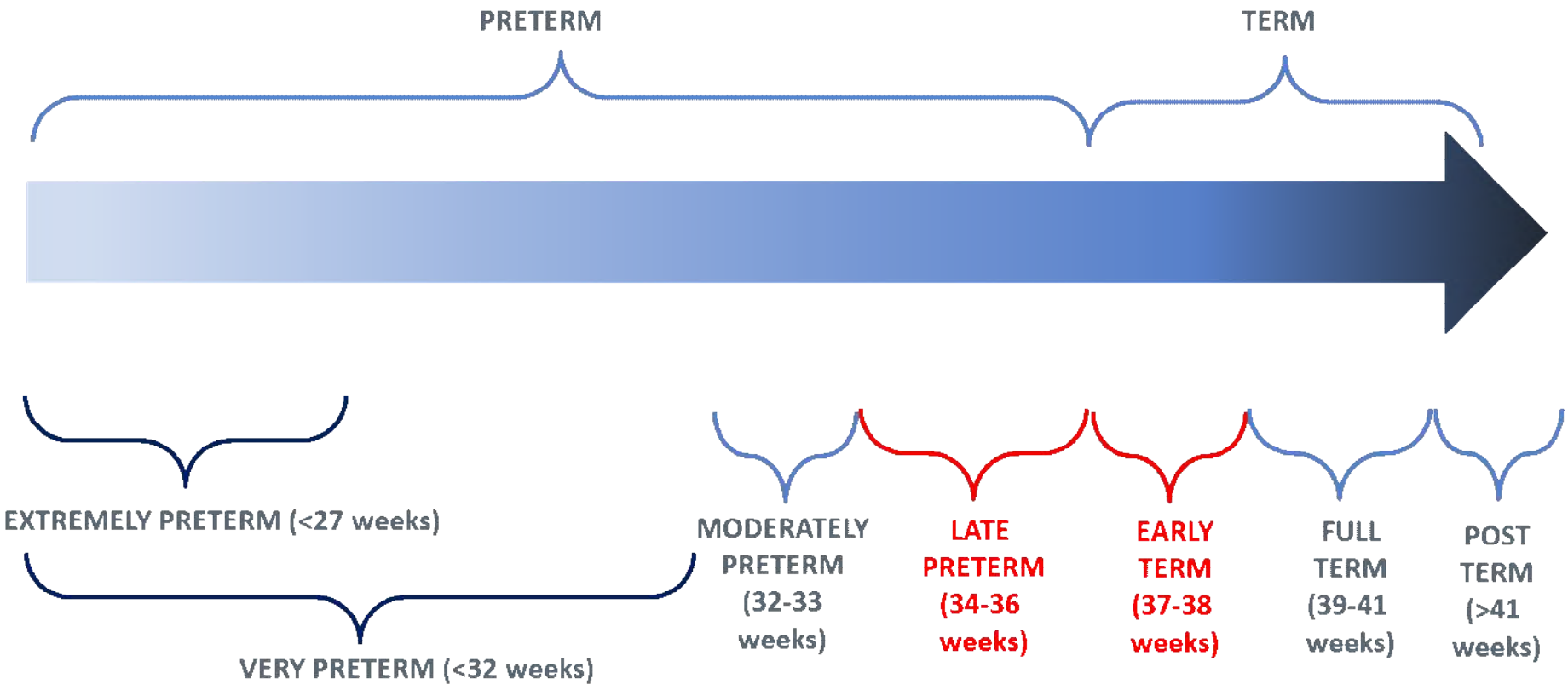
- Definitions
- SAEs & reporting
- Incident reporting & breaches

HOSPITAL TRANSFERS

PART I – Study Overview & Procedures

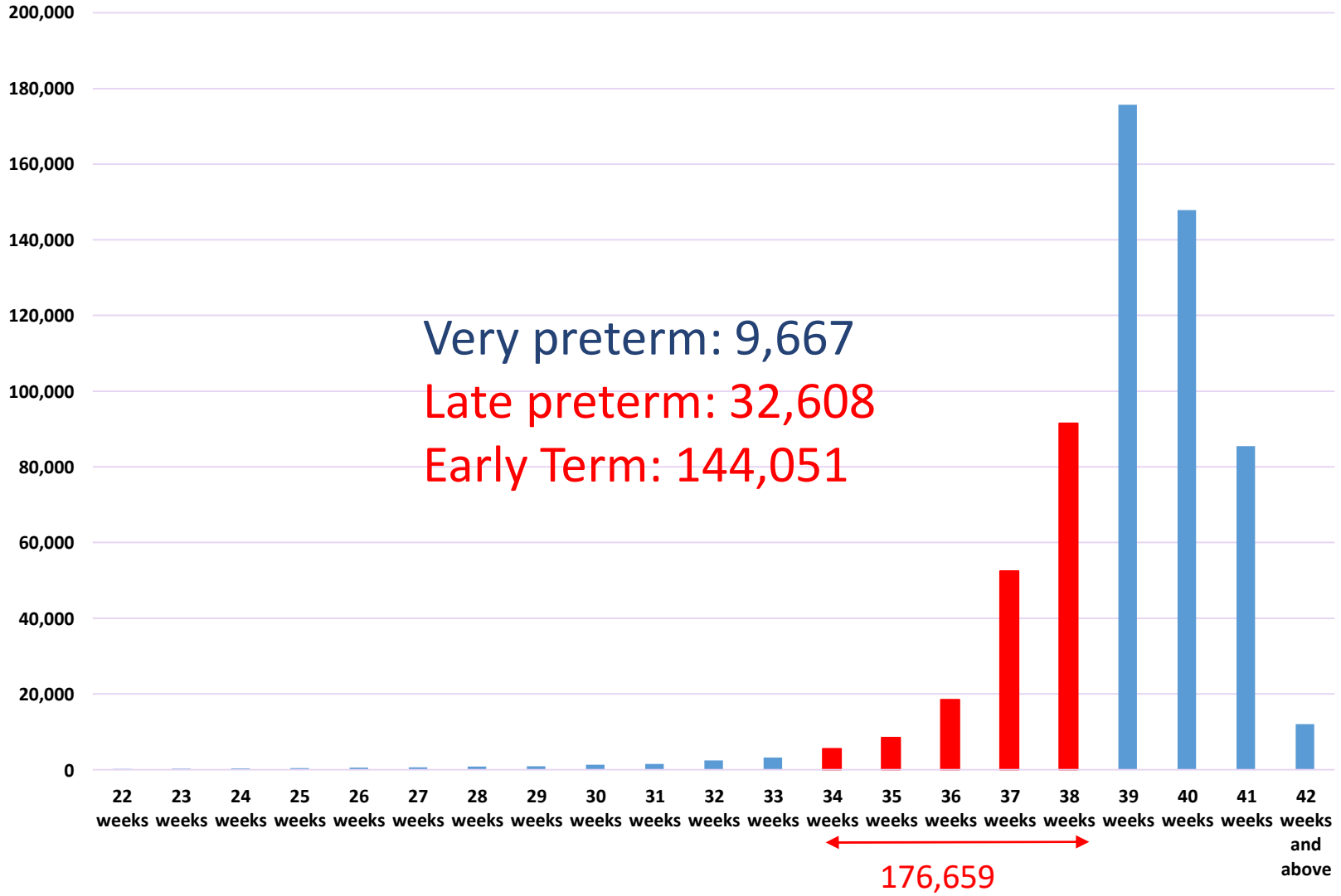
Safety Reporting & Hospital Transfers

Background & rationale for study



Gestational age

Live births by week of gestation (England and Wales 2020)



Neonatal Morbidities

- Common
- Relatively unrecognised until the last 10 -15 years
- Generally less severe than very preterm counterparts
- Often managed like full term infants
- Around 30-40% need specialist neonatal input
- Mostly related to poor feeding and metabolic immaturity
- Substantial burden of respiratory disease
- Most common diagnosis is RDS

Boyle et al. *Arch Dis Child Fetal Neonatal Ed* 2015

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Current practice

- Variable between and within neonatal units
- Some clinicians treat early with surfactant to prevent deterioration
- Some prefer to adopt a ‘watch and wait’ approach
- No defined limits for intervention
- No evidence for either approach
- Both can be regarded as “standard care”
- No RCTs in this group of babies

Potential impacts of different approaches to management

- Prolonged separation of mother and baby
- Prolonged hospital stay
- Decreased successful breastfeeding
- Increased psychological stress for mother and family
- Transfer for higher level of care
- Higher costs of neonatal care
- Long-term respiratory problems?

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HYPOTHESIS

Early, proactive management of respiratory disease will

- reduce the progression to severe respiratory failure requiring mechanical ventilation
- reduce length of hospital stay
- reduce early hospital readmissions
- reduce costs of neonatal care

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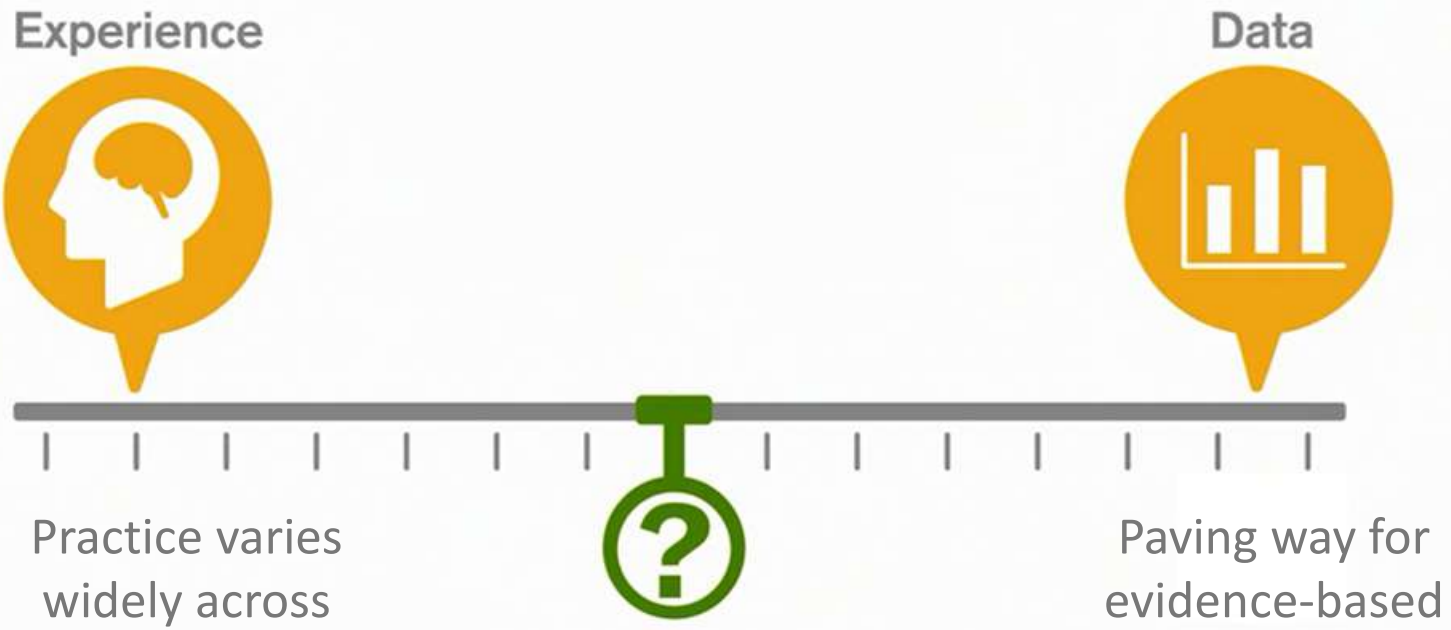

Study Objectives

- To compare **duration of neonatal hospital stay** in infants randomised to receive early surfactant versus those who received expectant management

- To compare **incidence of severe respiratory failure** in infants randomised to receive early surfactant therapy versus those who received expectant management

- To investigate the effects of early surfactant therapy versus expectant management on **perinatal secondary outcomes**

- To investigate the **cost-effectiveness** of early surfactant therapy versus expectant management

Study Design & Summary

- Study Design

Multicentre, open-label, randomised controlled trial

- Study Arms

Expectant management

Early surfactant therapy

- Sample Size

1,522 infants across UK in NICUs and LNUs.

SCUs are also now included following Substantial Amendment 07 approval

- Recruitment period

30 months of active recruitment was planned; Trial end date will be advised

- Follow up

Remote FU with no direct contact with participants at one year of age, corrected for prematurity

- Team

Study Coordinating centre – NPEU CTU, University of Oxford

Sponsor – University of Leicester

Funder – NIHR HTA Programme

Primary outcomes

1. Length of infant's hospital stay after birth, defined as,
   the number of days from birth to discharge home from hospital

2. Incidence of severe respiratory failure, defined as,
   sustained (≥ 30 minutes) requirement for $FiO_2 \geq 0.45$ to maintain $SaO_2 \geq 92\%$

Secondary outcomes

Perinatal clinical outcomes

- Duration of NNU stay
- Intensive care support
- Mechanical ventilation
- Non-invasive respiratory support
- Pulmonary air leaks requiring chest drain
- Days of mother-infant separation
- Breast milk feeding
- Late onset sepsis
- iNO and ECMO therapy
- Respiratory diagnoses
- Surfactant administration
- Maternal length of hospitalisation

Health economics

- Cost of maternal hospitalisation
- Self-reported maternal health-related quality of life
- Costs associated with neonatal care
- Paediatric secondary care use and associated costs

Study Criteria

Inclusion criteria

1. Born at 34^{+0}–38^{+6} weeks of gestation
2. ≤ 24 hours old
3. Respiratory distress, defined as:
   - FiO_2 ≥ 0.3 and < 0.45 to maintain oxygen saturations SaO_2 ≥ 92%

   or

   - Clinically significant work of breathing, regardless of FiO_2
4. Clinical decision to provide non-invasive respiratory support
5. Written parental informed consent

Exclusion criteria

1. Major structural or chromosomal abnormality
2. No realistic prospect of survival
3. Prior intubation and/or surfactant administration
4. Known or suspected hypoxic ischaemic encephalopathy
5. Congenital abnormality of the respiratory tract
6. Known or suspected neuromuscular disorder

PART I – Study Overview & **Procedures**

Safety Reporting & Hospital Transfers

Current Protocol:

SurfON Protocol V6.0
Dated 31 March 2022

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Trial Title: Multicentre, open-label, randomised controlled trial of early surfactant therapy versus expectant management in late preterm and early term infants with respiratory distress.

Short title: SurfON – Surfactant Or Not

Ethics Ref: 20/EM/0003

IRAS Project ID: 269023

Sponsor Ref: UOL 0727

EudraCT Number: 2019-003764-45

Date and Version No: 31 March 2022 and 6.0

Chief Investigator:

Professor Elaine M Boyle
Professor in Neonatal Medicine
College of Life Sciences
University of Leicester
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0116 252 5447

Sponsor:

University of Leicester

Research Governance Office
Research & Enterprise Division
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0116 258 4099/4867

Funder:

National Institute for Health Research (NIHR) Health Technology Assessment (HTA) Programme (17/89/07)

NIHR National Institute for Health Research | University of Leicester | NPEU Clinical Trials Unit | Oxford Population Health NPEU

Schedule of Trial Procedures

PROCEDURES	BEFORE TRIAL ENTRY	AFTER TRIAL ENTRY				
	Screening	Baseline	Randomisation	Intervention	Data collection	
	Within ≤ 24 hours of birth			Post-randomisation	At hospital discharge	At one year of age
Eligibility assessment	X					
Informed consent		X				
Randomisation			X			
Surfactant administration				X		
Questionnaires		X			X	
Perinatal clinical data collection		X	X	X	X	
Follow-up data collection using routine national database						X
Adverse events assessments (SAEs, SUSARs etc)			X	X	X	

Screening & Eligibility Checks

Maternity ward

Image courtesy: Bedford Hospital NHS Trust

Neonatal Units

Image courtesy: Telegraphy; Queen Charlotte & Chelsea Hospital

Inclusion Criteria

SurfON

1. Born at 34^{+0}– 38^{+6} weeks of gestation
2. ≤ 24 hours old
3. Respiratory distress defined as:
   - FiO_2 ≥ 0.3 and < 0.45 needed to maintain SaO_2 ≥ 92%, or
   - Clinically significant work of breathing, regardless of FiO_2
4. Clinical decision to provide non-invasive respiratory support
5. Written parental informed consent

SurfON Inclusion Exclusion Criteria Card v1.0, 4-Jun-2020

Exclusion Criteria

SurfON

1. Major structural or chromosomal abnormality
2. No realistic prospect of survival
3. Prior intubation and/or surfactant administration
4. Known or suspected hypoxic ischaemic encephalopathy
5. Congenital abnormality of the upper or lower respiratory tract
6. Known or suspected neuromuscular disorder

www.npeu.ox.ac.uk/surfon surfon@npeu.ox.ac.uk

SurfON Inclusion Exclusion Criteria Card v1.0, 4-Jun-2020

Screening & Eligibility Checks

- ✓ Aim to approach parents early after infant's admission, when respiratory distress occurs (*can be before inclusion criteria reached*)
- ✓ Women expected to deliver at 34-36 weeks may be made aware of the study prior to delivery, at the clinical team's discretion. Liaise with maternity unit staff to make sure that they are familiar with the study
- ✓ Please include all pregnant women or infants screened in the **Screening Log**, even if they decline participation (avoid duplications!)
- ✓ Screening can be completed by any trained staff member
- ✓ However, eligibility will be reconfirmed at the point of consent & randomisation by *delegated medically trained doctor & ANNPs*
- ✓ Where parents do not have a good understanding of English, sites may use the translation and interpreting services, which they routinely use in clinical practice to communicate about the trial.

RECRUITMENT Hints and Tips

SurfON

Early Approach is Key!

Times when it may be appropriate to approach parents about SurfON

- If you are admitting a baby who meets the gestation criteria because they are exhibiting signs of respiratory distress, regardless of a need for respiratory intervention at this point
- If you are counselling a mother whose baby is being delivered late preterm or early term and there is suspicion the infant may need neonatal unit admission

Times when it may be appropriate to approach and consent, but not randomise to SurfON

- If the baby has an oxygen requirement, regardless of a decision to commence non-invasive respiratory support
- If the infant is on ncpap or high flow, but is in less than 30% oxygen and does not have clinically significant work of breathing

Times when it is appropriate to consent and randomise to SurfON

- If the infant is on ncpap or highflow and has significant work of breathing, regardless of oxygen requirement
- If the infant meets the entry criteria, but enrolment may mean the infant could subsequently need transferring out

SurfON Posters & Stickers to act as visible approach/recruitment reminders!

Parent-friendly podcast for sharing

Introduction to...

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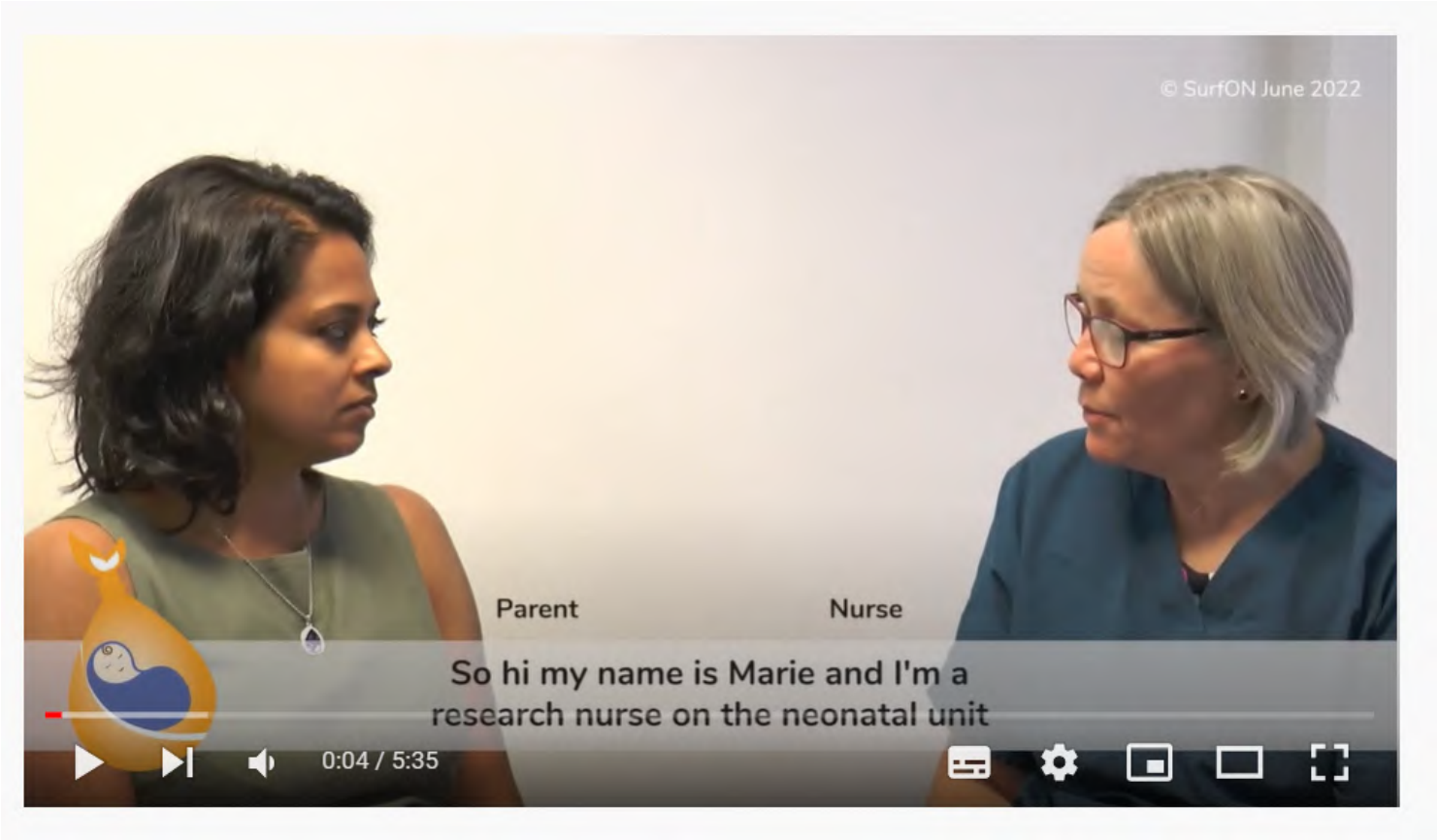
Early approach with parents



Direct link for training staff members - https://www.youtube.com/watch?v=eOZuARryrK8
Website - https://www.npeu.ox.ac.uk/surfon/clinicians/training-materials

SurfON – Exploring current evidences and practices

Dr Charles Roehr, Clinical Director NPEU CTU and Professor Elaine M Boyle, Chief Investigator

Involving Bigger Babies in Research

Prof Elaine Boyle & Dr Shalini Ojha

Training podcasts and further resources for use at internal training events, grand rounds etc:
https://www.npeu.ox.ac.uk/surfon/clinicians/podcasts
https://www.npeu.ox.ac.uk/surfon/clinicians/resources
https://www.npeu.ox.ac.uk/surfon/clinicians/training-materials

Roll up Banner & Posters

RAISE AWARENESS

Participant Information Leaflet (PIL)

V3.0 27th May 2020

PIL will be personalised to include local contact details for the site

Who is organising and funding the study?

The study is funded by the National Institute of Health Research (NIHR) [Health Technology Assessment (HTA) programme (Project reference 17/89/07)].

The study is sponsored by the University of Leicester, and will be run by the National Perinatal Epidemiology Unit Clinical Trials Unit (NPEU CTU) at the University of Oxford.

All research in the NHS is looked at by an independent group of people, called a Research Ethics Committee, to protect your interests. This trial has been reviewed and given favourable opinion by East Midlands - Derby Research Ethics Committee.

Further information:

We will send you a copy of the results at the end of the study and we will also share them on our website. If at any time you have concerns about this study, please speak with the doctors looking after your baby or contact the Sponsor at *rgosponsor@leicester.ac.uk*. In the event that something does go wrong and you are harmed during the research and this is due to someone's negligence then you may have grounds for a legal action for compensation against the Sponsor but you may have to pay your legal costs. The normal National Health Service complaints mechanisms will still be available to you (if appropriate).

If you would like to contact an independent organisation, we suggest that you contact Bliss, a special care baby charity.

Bliss for babies born premature or sick
https://www.bliss.org.uk
020 7378 1122
hello@bliss.org.uk

The Patient Advice and Liaison Service (PALS) is a confidential NHS service that can provide you with support that you may have regarding the care you receive as an NHS patient.

Contact Information:

Chief Investigator:
Prof. Elaine M Boyle
ebl24@leicester.ac.uk

Local Contact Details

Principal Investigator:
<insert name>
<Insert contact details>

Local Research Nurse:
<insert name>
<Insert contact details>

[PALS]
<insert name>
<Insert contact details>

SurfON Study Team

NPEU Clinical Trials Unit, University of Oxford,
Old Road Campus, Headington, Oxford, OX3 7LF.
01865 289437 / 738 / 599
surfon@npeu.ox.ac.uk
www.npeu.ox.ac.uk/surfon

This study is funded by the National Institute for Health Research (NIHR) [Health Technology Assessment (HTA) (project reference 17/89/07)]. The views expressed are those of the author(s) and not necessarily those of the NIHR or the Department of Health and Social Care.

REC Ref: 20/EM/0003 IRAS ID: 269023

FUNDED BY: NIHR National Institute for Health Research
UNIVERSITY OF LEICESTER
NPEU Clinical Trials Unit
UNIVERSITY OF OXFORD

SurfON
Surfactant Or Not

For babies born early with breathing problems

Multicentre, open-label, randomised controlled trial of early surfactant therapy versus expectant management in late preterm and early term infants with respiratory distress.

Participant Information Leaflet (PIL)

One PIL for use across nations - Scotland, England, Wales & Northern Ireland
Available on SurfON website - https://www.npeu.ox.ac.uk/surfon

Parent Information Leaflet

Thank you for taking the time to read about this research study. We would like to invite you and your baby to take part in the SurfON study. This leaflet explains why we are doing this study and what it means for you and your baby. We know this is a stressful time for you and your family. Please feel free to discuss this with your family. We are happy to answer any questions.

What is the purpose of the study?

This study is about babies born two to six weeks before their due date. Babies born even a few weeks early are not fully developed. These babies may have breathing problems after birth, which can be severe. Some need to go onto a breathing machine (ventilator) soon after birth; others do not, but still need some help with breathing. They often go onto 'non-invasive' breathing support, which means that machines give oxygen through soft, short tubes in the nose or small masks over the nose.

The lungs of healthy full term babies naturally produce surfactant. This is a substance made up of proteins and fats that helps to keep the tiny air sacs in the lungs open, making it easier for them to breathe. Babies born early often do not make enough natural surfactant, or their surfactant does not work properly. As a result, babies may have difficulty expanding their lungs to take in oxygen. We can give a natural, animal-derived surfactant medication into the lungs, using a small tube put into the windpipe through the mouth. We do this routinely soon after birth in many babies born more than 10 weeks early to help their breathing.

At the moment, there have been no research studies into the timing of giving surfactant in babies born closer to term with breathing problems, so we have no guidance on this. Whilst some doctors prefer to use surfactant early, others do not, so clinical practice varies widely across hospitals in the UK. For this reason, we would like to know if it is better to give surfactant early, when a baby first starts to have problems, or see if they will improve without it.

Why are we being invited to take part?

Your baby was born between two and six weeks early and needs help with breathing.

Do we have to take part?

No, it is entirely up to you. If you decide not to take part, this will not affect your care or your baby's care. If you take part and then change your mind, you are free to withdraw at any time, although data collected up until withdrawal will be used in the study. You can withdraw by speaking to your baby's doctor. You do not have to give a reason.

What will happen if we take part?

We will ask you to sign a consent form. Your baby will be put into one of two groups, which will be decided by a computer program at random. There will be an equal chance of your baby being in either group. Babies in one group will receive a single dose of surfactant when they first start to need help breathing. In the other group the doctor will see if their breathing improves with non-invasive support alone. Regardless of which group your baby is in, they may still receive surfactant, if the doctor feels it becomes necessary.

We will collect some information about you and your baby such as length of stay in hospital, duration of non-invasive support and breast milk feeding from medical records. We will ask you to fill in a short questionnaire after you give consent and just before your baby leaves the hospital. We will also collect information through NHS digital or an equivalent national database, relating to survival and any hospital visits your baby has in their first year.

What are the possible disadvantages and risks from taking part?

Surfactant is routinely used in babies and there are no extra risks involved from taking part in the study.

What are the benefits from taking part?

Whilst there may not be any direct benefit in taking part in the study, your participation will be invaluable to help improve future care for these babies.

What will happen to the information collected about us during the study?

All information that we collect about you and your baby during the study will be kept strictly confidential and stored securely. You and your baby will not be identifiable in any publications of the results or reports from this study.

If you decide to take part, we will collect some personal information about you and your baby, including name, address and contact details. This information will be sent to the Study Coordinating Centre at the University of Oxford, National Perinatal Epidemiology Unit Clinical Trials Unit (NPEU CTU). Authorised members of the research team will hold this data and store it securely. Authorised staff from the University of Oxford (as Coordinating Centre) and University of Leicester (as Sponsor), funder, regulatory bodies, and your hospital may be given access to data for monitoring and/or audit of the study to ensure the research is complying with applicable regulations. Personal identifiable information including name, address, date of birth, gender and healthcare number will be shared with NHS digital or an equivalent national database.

The Study Coordinating Centre in Oxford will keep identifiable information about you and your baby from this study for 25 years after the study has finished.

Only anonymised information from this study may be shared with other researchers doing similar research in the future. None of your personal identifiable information will be shared with other researchers.

For more information on how we process and protect you and your baby's data, please see our website: **https://npeu.ox.ac.uk/ctu/privacy-notice**

Further information can also be found at the NHS Health Research Authority's website:

SCAN QR CODE

SurfON

NHS Health Research Authority

SurfON General Data Protection Regulation (GDPR) for Patients

Study Title: Multicentre, open-label, randomised controlled trial of early surfactant therapy versus expectant management in late preterm and early term infants with respiratory distress.

Chief Investigator: Professor Elaine M Boyle

Patient data and research

This leaflet explains how health research uses information from patients. If you are asked to take part in research, you can ask what will happen in the study.

What is patient data?

When you go to your GP or hospital, the doctors and others look[ed] information about your health. This will include your health problems, a[nd] have had. They might want to know about family history, if you s[ee] formation that is recorded about you is called patient data.

When information about your health care [is] (like your name or NHS number) it is [called] of us that this identifiable patient info[rmation] to need to know relevant bits of that [information] to keep confidential patient inform[ation].

What sort of [research]

There are [many] If you take p[art] [in] a medicine or other treatment. Or you may take part [in] some health tests or answer some questions. When you have [finished] the research team may look at your medical history and ask you ques[tions] [re]levant for the study. During the study you may have blood tests or other healt[h] may complete questionnaires. The research team will record this data in special fo[rms] combine it with the information from everyone else in the study. This recorded information is research data.

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

Paper copy only upon request

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Schedule of Trial Procedures

PROCEDURES	BEFORE TRIAL ENTRY	AFTER TRIAL ENTRY				
	Screening	Baseline	Randomisation	Intervention	Data collection	
		Within ≤ 24 hours of birth		Post-randomisation	At hospital discharge	At one year of age
Eligibility assessment	X					
Informed consent		X				
Randomisation			X			
Surfactant administration				X		
Questionnaires		X			X	
Perinatal clinical data collection		X	X	X	X	
Follow-up data collection using routine national database						X
Adverse events assessments (SAEs, SUSARs etc)			X	X	X	

Informed Consent

- Consent and randomisation should be carried out ≤ 24 hours of birth.
- Final assessment of eligibility of the infant for SurfON, must be confirmed by delegated clinician or ANNP at the point of randomisation.
- *Clinicians, ANNPs & nurses* can obtain consent, but do check if this is in line with your trust policy. The staff member must be signed off by the local Principal Investigator (PI) on SurfON Site Delegation Log to perform this responsibility
- Parents are made aware that participation is voluntary
- Parent with legal parental responsibility for the infant must sign consent to the study. Where the mother is under 16 years of age, she may be approached for consent by the medical team, if she is determined to be competent according to the Fraser Guidelines.

V4.0 31st Mar 2022

Parent Consent Form

SurfON
Surfactant Or Not

Please complete in black ballpoint pen

Chief Investigator: Professor Elaine M Boyle

Multicentre, open-label, randomised controlled trial of early surfactant therapy versus expectant management in late preterm and early term infants with respiratory distress.

Hospital name: Leicester Royal Infirmary Study number: 10083

Baby's first name (BLOCK CAPITALS): MARLEY (TWIN ONE)

Baby's last name (BLOCK CAPITALS): BOB

PLEASE INITIAL BOX

1. I confirm that I have read the SurfON Parent Information Leaflet (Version 3.0, 27/05/2020) for this study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily. — DM
2. I understand that participation is voluntary and that I am free to withdraw my baby and myself from the study at any time without giving any reason, and that our present or future medical care or legal rights will not be affected. — DM
3. I understand that relevant sections of medical records and data collected during the study relating to me or my baby may be looked at by staff from the research team, sponsor, funder, regulatory authorities and this NHS Trust. I give permission for these individuals to have access to these records where it is relevant to taking part in this research. — DM
4. I agree to personal identifiable information relating to myself and/or my baby being collected, stored and used by the coordinating centre (NPEU CTU) in the University of Oxford. This is on the understanding that any information will be treated confidentially. — DM
5. I agree that personal identifiable information including name, address, date of birth, gender and healthcare number can be shared with national databases such as NHS Digital or equivalent, in order to collect information relating to survival and any hospital visits my baby has in their first year. — DM
6. I agree to my baby taking part in this study. LEAH MARLEY 05/05/22 — DM

Name of parent (IN BLOCK CAPITALS)	Signature	
DAVID MARLEY		04/05/22
Name of delegated health professional taking consent: ROSE GARR		04/05/22

IMPORTANT: PLEASE OBTAIN THE MOTHER'S COUNTERSIGNATURE AS SOON AS POSSIBLE IF OTHER PARENT HAS PROVIDED ORIGINAL CONSENT.

MOTHER: PLEASE INITIAL BOX

7. I agree to complete short study questionnaires. — LM
8. I agree to take part in the study — LM

Optional:

9. I agree to be contacted in the future about further research related to this study. —

Name of mother (IN BLOCK CAPITALS)	Signature	
LEAH MARLEY		05/05/22
Name of delegated health professional taking consent: ROSE GARR		05/05/22

MOTHER CAN COMPLETE QUESTIONNAIRES ONLY IF CONSENT HAS BEEN PROVIDED IN THE SECTION ABOVE. HEALTH PROFESSIONAL MUST ALSO SIGN.

SurfON Study Team, NPEU CTU, National Perinatal Epidemiology Unit, Nuffield Department of Population Health, University of Oxford, Old Road Campus, Oxford, OX3 7LF.
01865 289 437/738 01865 289 740 ouh-tr.surfon@nhs.net www.npeu.ox.ac.uk/surfon

FUNDED BY NIHR | National Institute for Health Research

After consent, obtain a Study No from the Randomisation website and write Study No here

Differentiate between multiples (for example, infants can be named as TWIN ONE, TWIN TWO).

Where first name is not yet confirmed, write down as Baby.

Initial the box, not tick

Both the parent providing consent and the health professional taking consent must be on the same date.

Mother should counter-sign even if the other parent provides consent initially

Consent to complete questionnaire does not affect taking part in the main study

Optional consent and can be left blank if they do not wish to be contacted in the future

Original in the Investigator Site File (ISF);
1x copy to be given to the Parent and 1x copy to be stored in the infant's medical notes.

V4.0 31st Mar 2022

Parent Consent Form

SurfON
Surfactant Or Not

Please complete in black ballpoint pen

Chief Investigator: Professor Elaine M Boyle

Multicentre, open-label, randomised controlled trial of early surfactant therapy versus expectant management in late preterm and early term infants with respiratory distress.

Hospital name: Leicester Royal Infirmary Study number: 1 0 0 8 3

Baby's first name (BLOCK CAPITALS): MARLEY (TWIN ONE)

Baby's last name (BLOCK CAPITALS): BOB

	PLEASE INITIAL BOX
1. I confirm that I have read the SurfON Parent Information Leaflet (Version 3.0, 27/05/2020) for this study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily.	DM
2. I understand that participation is voluntary and that I am free to withdraw my baby and myself from the study at any time without giving any reason, and that our present or future medical care or legal rights will not be affected.	DM
3. I understand that relevant sections of medical records and data collected during the study relating to me or my baby may be looked at by staff from the research team, sponsor, funder, regulatory authorities and this NHS Trust. I give permission for these individuals to have access to these records where it is relevant to taking part in this research.	DM
4. I agree to personal identifiable information relating to myself and/or my baby being collected, stored and used by the coordinating centre (NPEU CTU) in the University of Oxford. This is on the understanding that any information will be treated confidentially.	DM
5. I agree that personal identifiable information including name, address, date of birth, gender and healthcare number can be shared with national databases such as NHS Digital or equivalent, in order to collect information relating to survival and any hospital visits my baby has in their first year.	DM
6. I agree to my baby taking part in this study. LEAH MARLEY 05/05/22	DM

Name of parent (IN BLOCK CAPITALS): DAVID MARLEY	Signature	0 4 / 0 5 / 2 2
Name of delegated health professional taking consent: ROSE GARR	Signature	0 4 / 0 5 / 2 2

IMPORTANT: PLEASE OBTAIN THE MOTHER'S COUNTERSIGNATURE AS SOON AS POSSIBLE IF OTHER PARENT HAS PROVIDED ORIGINAL CONSENT.

MOTHER:	PLEASE INITIAL BOX
7. I agree to complete short study questionnaires.	LM
8. I agree to take part in the study	LM
Optional:	
9. I agree to be contacted in the future about further research related to this study.	

Name of mother (IN BLOCK CAPITALS): LEAH MARLEY	Signature	0 5 / 0 5 / 2 2
Name of delegated health professional taking consent: ROSE GARR	Signature	0 5 / 0 5 / 2 2

MOTHER CAN COMPLETE QUESTIONNAIRES ONLY IF CONSENT HAS BEEN PROVIDED IN THE SECTION ABOVE. HEALTH PROFESSIONAL MUST ALSO SIGN.

SurfON Study Team, NPEU CTU, National Perinatal Epidemiology Unit, Nuffield Department of Population Health, University of Oxford, Old Road Campus, Oxford, OX3 7LF.
01865 289 437/738 01865 289 740 ouh-tr.surfon@nhs.net www.npeu.ox.ac.uk/surfon

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Consent to complete questionnaire does not affect taking part in the main study

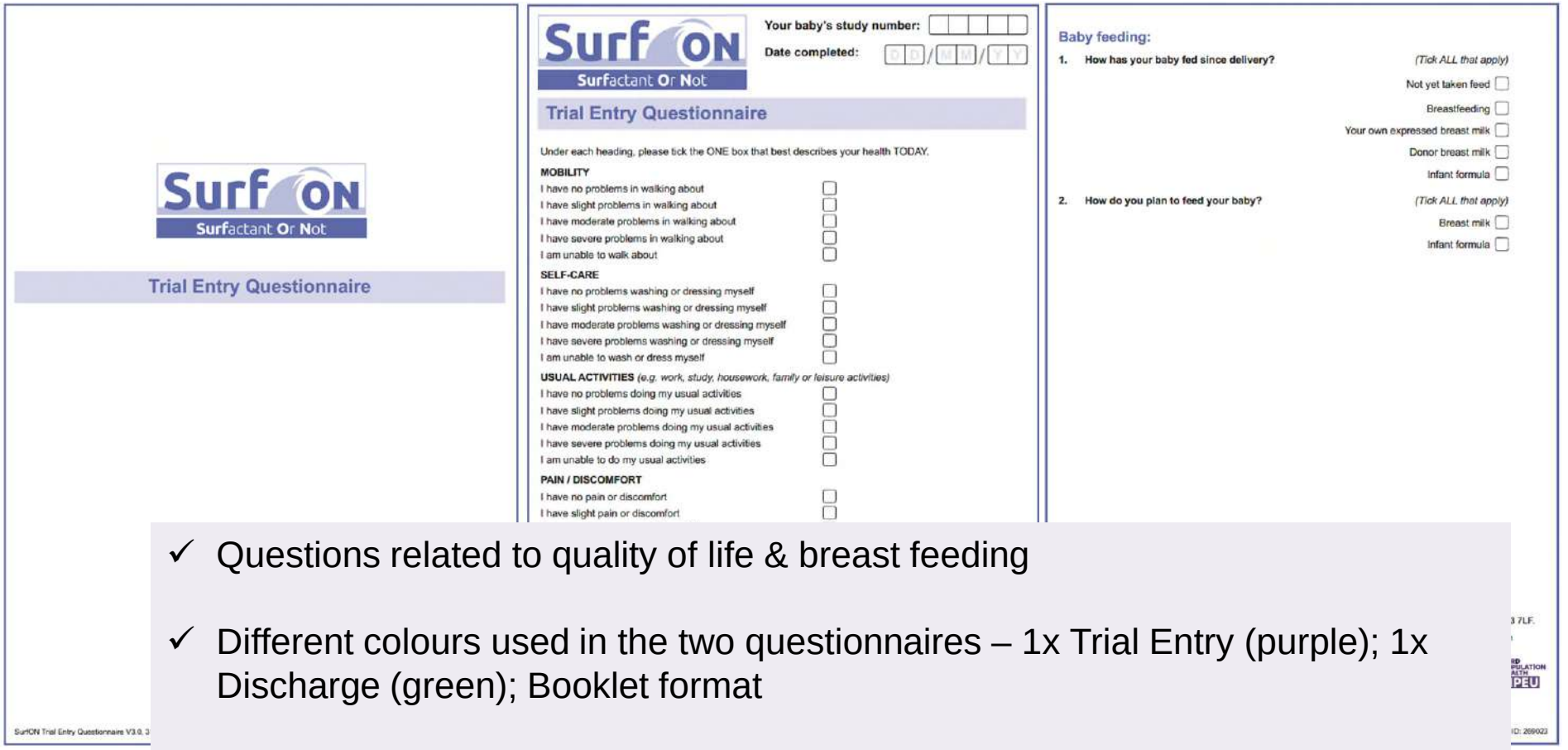
Optional consent and can be left blank if they do not wish to be contacted in the future

Original in the Investigator Site File (ISF);
1x copy to be given to the Parent and 1x copy to be stored in the infant's medical notes.

A clear scanned copy of the original should be uploaded via the NPEU Document Upload Tool

Administer Trial Entry Questionnaire

V4.0 31st Mar 2022



- ✓ Questions related to quality of life & breast feeding
- ✓ Different colours used in the two questionnaires – 1x Trial Entry (purple); 1x Discharge (green); Booklet format
- ✓ If the mother has delivered multiple infants, a questionnaire should be completed for each infant, for example, if the mother has delivered twins, she would complete 2x Trial Entry Questionnaires.

Both Trial Entry and Trial Discharge questionnaires should be entered onto OpenClinica; Original should be filed in the **Data Collection File**

Provide Thank You Card

SurfON Cot card

SurfON Randomised Sticker

Schedule of Trial Procedures

PROCEDURES	BEFORE TRIAL ENTRY	AFTER TRIAL ENTRY				
	Screening	Baseline	Randomisation	Intervention	Data collection	
	Within ≤ 24 hours of birth			Post-randomisation	At hospital discharge	At one year of age
Eligibility assessment	X					
Informed consent		X				
Randomisation			X			
Surfactant administration				X		
Questionnaires		X			X	
Perinatal clinical data collection		X	X	X	X	
Follow-up data collection using routine national database						X
Adverse events assessments (SAEs, SUSARs etc)			X	X	X	

Randomisation

- ✓ Final assessment of eligibility of the infant for SurfON, must be confirmed by delegated clinician or ANNP at the point of randomisation.
- ✓ Randomisation Website -https://rct.npeu.ox.ac.uk/surfon/login.php

Randomisation 1:1

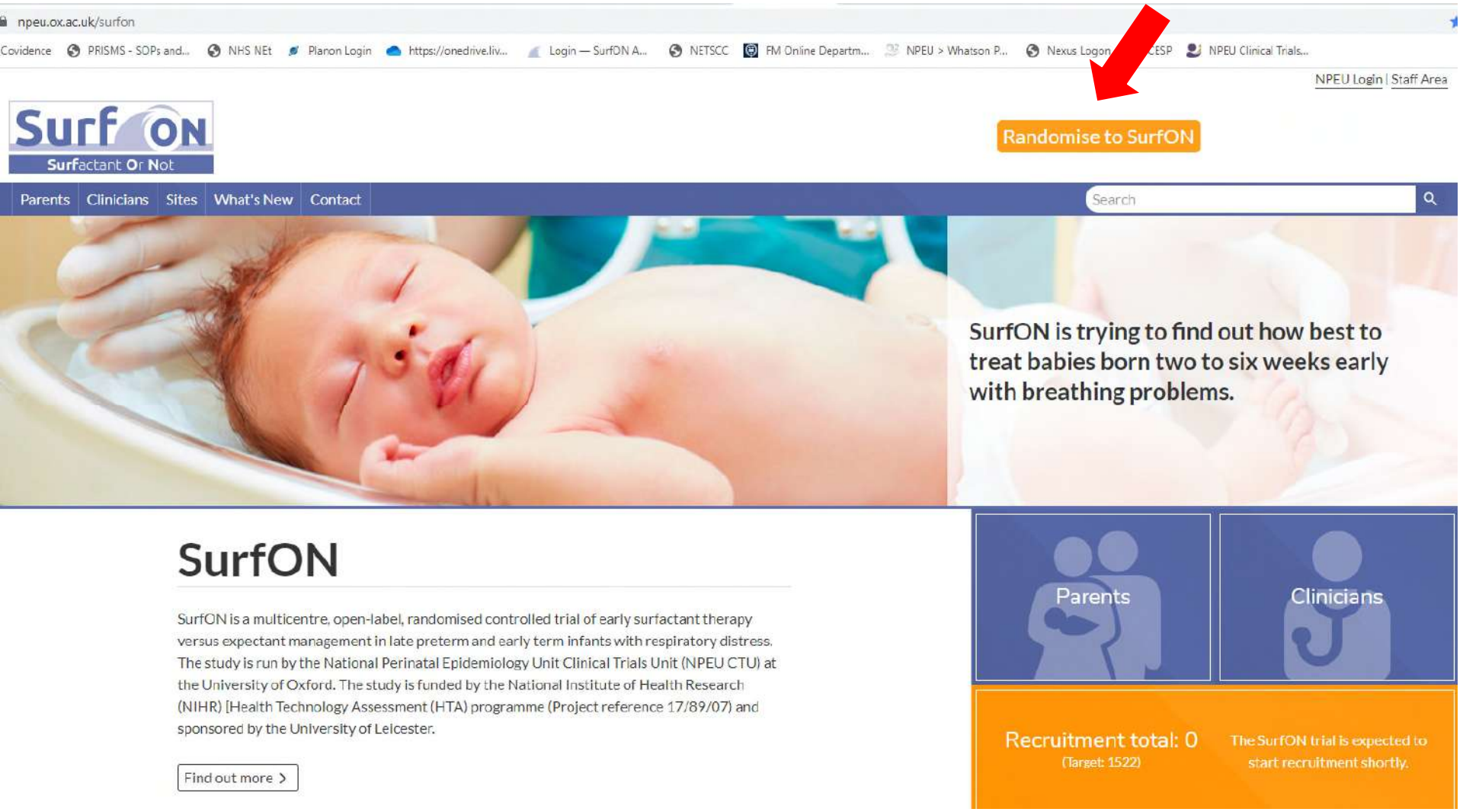
≤ 24 hours birth

Expectant Management

Early Surfactant Therapy

Multiples randomised to the same arm

Randomisation



Randomisation Website -https://rct.npeu.ox.ac.uk/surfon/login.php

Demonstration version only

Randomisation Program

If you need to contact us **urgently** with randomisation problems, please click on this **link**

Logged in as: **Centre 1 (City 1)**

Menu

- **Enter infant**
- **Recruitment list**
- **Screening log**
- **Add infant to screening log**

- **Log out**

Centre Log-in will be provided after completion of training

SurfON

Demonstration version only

Randomisation Program

Section A: Eligibility

Time of randomisation: 16 Jun 2020 13:46

Press **Complete** to confirm randomisation or **Amend** to change any values

Complete | Amend | Cancel

A1. What was the expected date of delivery (EDD)?	25 / June / 2020
A2. What is the infant's date of birth?	15 / June / 2020
	17 : 33 24hr clock
A3. What is the infant's sex?	Male
A4. What is the FiO_2 needed to maintain $SaO_2 \geq 92\%$?	0.4
A5. Is the work of breathing clinically significant, regardless of FiO_2?	Yes
A6. Is there a clinical decision to provide non-invasive respiratory support?	Yes
A7. Do you have written parental informed consent for the infant's participation?	Yes
Who signed the consent form?	Mother
A8. Do you have written consent for the mother's participation to complete questionnaires?	Yes
A9. Does the infant have a major structural or chromosomal abnormality?	No
A10. Does the infant have no realistic prospect of survival?	No
A11. Has the infant had prior intubation and/or surfactant administration?	No
A12. Does the infant have known or suspected hypoxic ischaemic encephalopathy?	No
A13. Does the infant have a congenital abnormality of the upper or lower respiratory tract?	No
A14. Does the infant have a known or suspected neuromuscular disorder?	No
A15. Was the infant one of a multiple pregnancy?	No
Name of person completing this form:	Rose Garr

After you click Continue,
check that the data are correct.
If any information is incorrect, click **"Amend"** and enter the corrected information before clicking **"Complete"**.

SurfON

Demonstration version only

Randomisation Program

If you need to contact us **urgently** with randomisation problems, please click on this **link**

Logged in as: **Centre 1 (City 1)**

Section B: Randomisation

SurfON study number:
10031

Allocation
Expectant management

Date and time of randomisation
16/06/2020 13:46

Study number obtained here should be entered on the consent form & any other associated documents such as the questionnaire

Please record study number **10031** on the Consent Form and any other trial documentation for this infant.

Please press the **Print** button below to generate a pdf which you should print out.

Print

Thank you for entering this infant into the SurfON study.
Please click the link below to log out

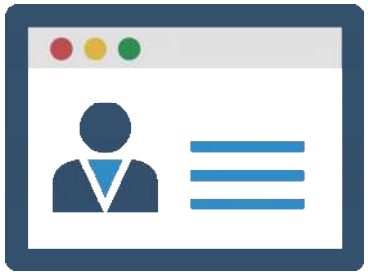
Log out

Home

Surf ON

Demonstration version only

Randomisation Program

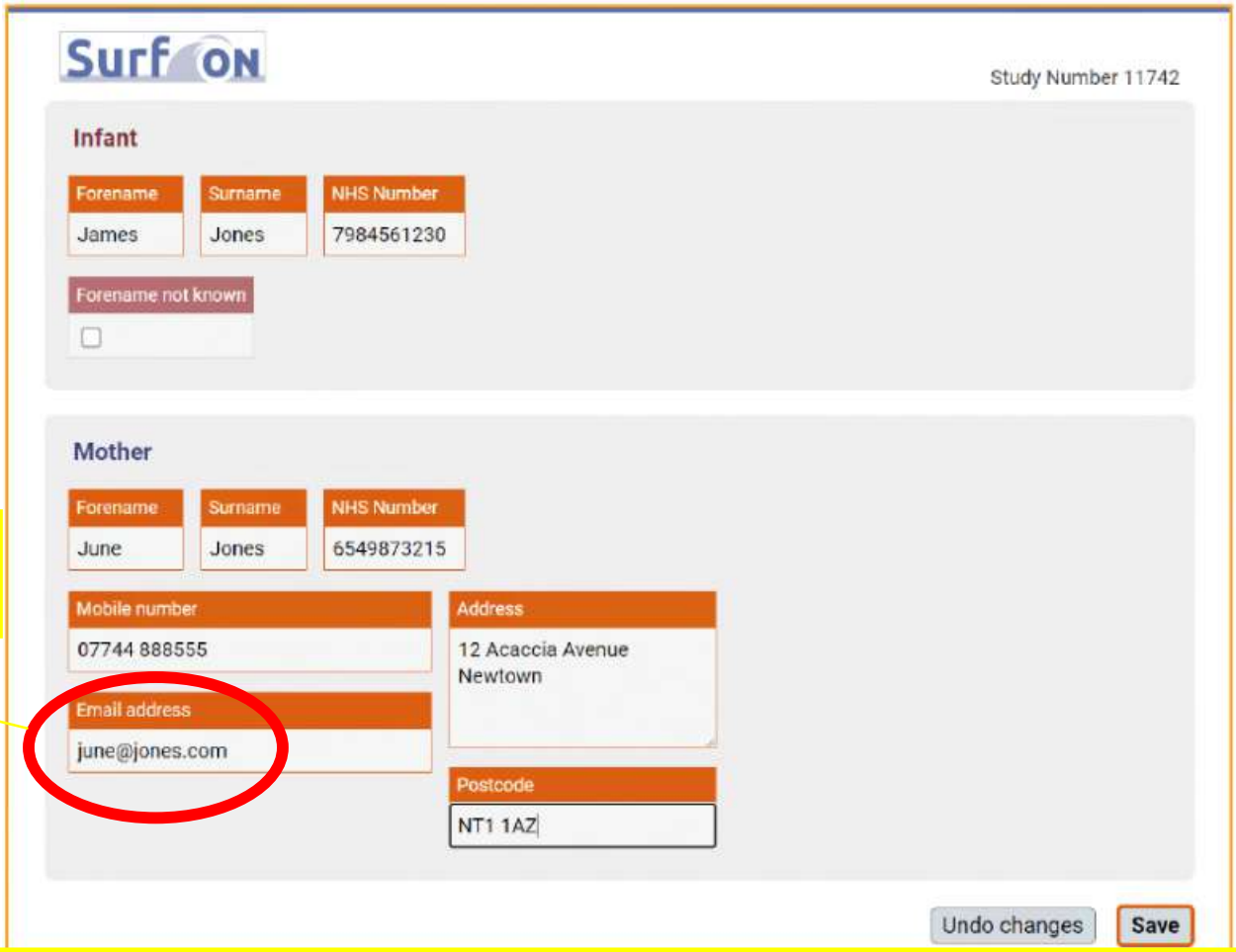


Contact Details Form

Study no	Time randomised	Allocation	Print	Edit contact details
10060	24/02/20 13:49	Early surfactant therapy	Print	Edit
10057	10/02/20 12:09		Print	Edit
10048	10/02/20 11:54		Print	Edit
10031	10/02/20 11:29		Print	Edit
10026	20/01/20 15:34		Print	Edit
10015	20/01/20 14:45		Print	Edit
Total 6				

Home

Contact Details Form



Email ID is often missing !

- ✓ Important to record infant & mother's healthcare number, email address, postal address and phone number
- ✓ **Trial Entry Form** (in Openclinica) is completed after Randomisation

Further details in Part II – Data Management

SurfON

SurfactantOr Not

Respiratory Support Log

NIHR | National Institute for Health Research

UNIVERSITY OF LEICESTER

NPEU Clinical Trials Unit

UNIVERSITY OF OXFORD

This study is funded by the National Institute for Health Research (NIHR) [Health Technology Assessment (HTA) (project reference 17/99/07)].
The views expressed are those of the author(s) and not necessarily those of the NIHR or the Department of Health and Social Care.

SurfON

Respiratory Support Log

NPEU Clinical Trials Unit

UNIVERSITY OF OXFORD

Day 1: D D / M M / Y Y

Study Number:

Date of birth: D D / M M / Y Y

Please complete this log for all infants in the SurfON study after randomisation for every day that the infant is receiving Respiratory support and/or Oxygen

Time interval	Respiratory Support (please tick ALL that apply)	Oxygen requirement: Did the infant require $FIO_2 \geq 0.46$ to maintain $SaO_2 \geq 92\%$ for a sustained period of ≥ 30 minutes?	Was surfactant administered? (please exclude single dose of surfactant given as study intervention)	Person completing entry (print name)
00:00 to 03:59	☐ Mechanical ventilation ☐ Positive airway pressure (CPAP, BIPAP) ☐ High Flow Therapy ☐ Incubator or low flow oxygen ☐ Breathing in air	Yes ☐ No ☐	Yes ☐ No ☐ *If Yes, please complete Surfactant Form*	
04:00 to 07:59	☐ Mechanical ventilation ☐ Positive airway pressure (CPAP, BIPAP) ☐ High Flow Therapy ☐ Incubator or low flow oxygen ☐ Breathing in air	Yes ☐ No ☐	Yes ☐ No ☐ *If Yes, please complete Surfactant Form*	
08:00 to 11:59	☐ Mechanical ventilation ☐ Positive airway pressure (CPAP, BIPAP) ☐ High Flow Therapy ☐ Incubator or low flow oxygen ☐ Breathing in air	Yes ☐ No ☐	Yes ☐ No ☐ *If Yes, please complete Surfactant Form*	
12:00 to 15:59	☐ Mechanical ventilation ☐ Positive airway pressure (CPAP, BIPAP) ☐ High Flow Therapy ☐ Incubator or low flow oxygen ☐ Breathing in air	Yes ☐ No ☐	Yes ☐ No ☐ *If Yes, please complete Surfactant Form*	
16:00 to 19:59	☐ Mechanical ventilation ☐ Positive airway pressure (CPAP, BIPAP) ☐ High Flow Therapy ☐ Incubator or low flow oxygen ☐ Breathing in air	Yes ☐ No ☐	Yes ☐ No ☐ *If Yes, please complete Surfactant Form*	
20:00 to 23:59	☐ Mechanical ventilation ☐ Positive airway pressure (CPAP, BIPAP) ☐ High Flow Therapy ☐ Incubator or low flow oxygen ☐ Breathing in air	Yes ☐ No ☐	Yes ☐ No ☐ *If Yes, please complete Surfactant Form*	

Sign off by delegated person

I confirm that I have checked the data recorded on this log against the infant's hospital records:

Name: *(Print)* _____ **Signature:** _____

Role: _____ **Date:** D D / M M / Y Y

SurfON Respiratory Support Log v1.0, 8-Jun-2020

01865 289 437/738/699 surfon@npeu.ox.ac.uk

Respiratory Support Log

Day 1: D D / M M / Y Y

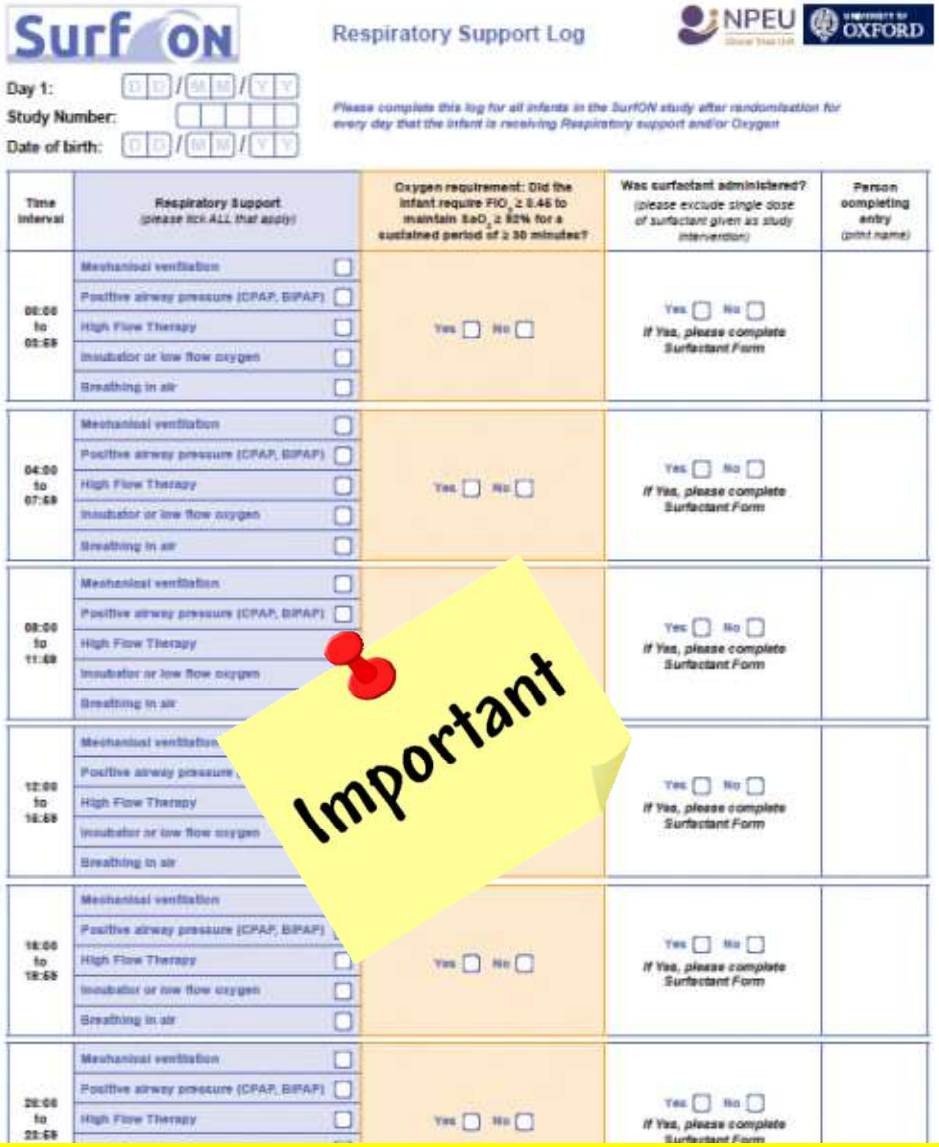
Study Number:

Date of birth: D D / M M / Y Y

Please complete this log for all infants in the SurfON study after randomisation for every day that the infant is receiving Respiratory support and/or Oxygen

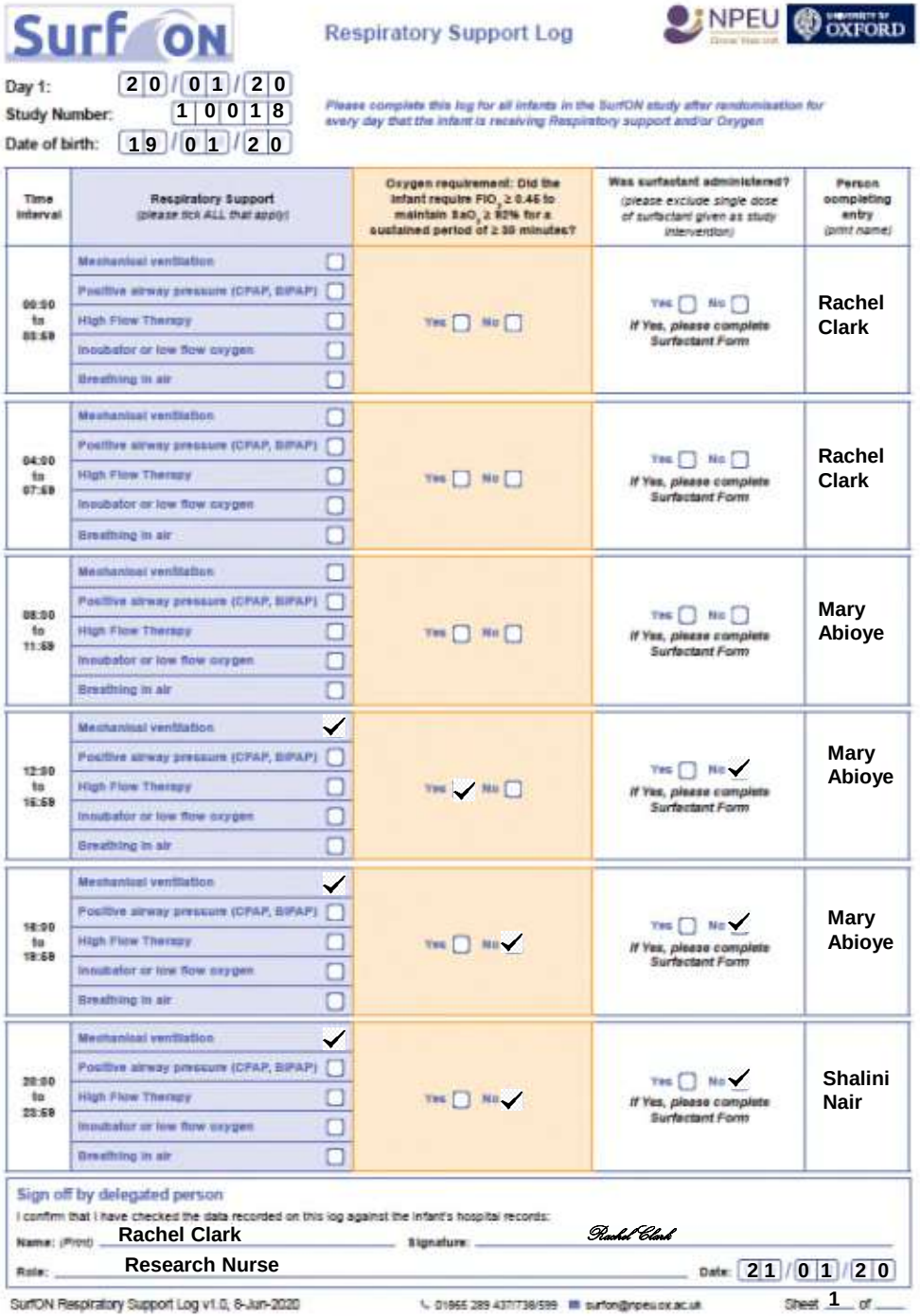
Time interval	Respiratory Support *(please tick ALL that apply)*	Oxygen requirement: Did the infant require $FiO_2 \geq 0.45$ to maintain $SaO_2 \geq 92\%$ for a sustained period of ≥ 30 minutes?	Was surfactant administered? *(please exclude single dose of surfactant given as study intervention)*	Person completing entry *(print name)*
00:00 to 03:59	Mechanical ventilation ☐ Positive airway pressure (CPAP, BiPAP) ☐ High Flow Therapy ☐ Incubator or low flow oxygen ☐ Breathing in air ☐	Yes ☐ No ☐	Yes ☐ No ☐ ***If Yes, please complete Surfactant Form***	
04:00 to 07:59	Mechanical ventilation ☐ Positive airway pressure (CPAP, BiPAP) ☐ High Flow Therapy ☐ Incubator or low flow oxygen ☐ Breathing in air ☐	Yes ☐ No ☐	Yes ☐ No ☐ ***If Yes, please complete Surfactant Form***	

Reports on **the primary outcome** for the study !



1. Reports on **the primary outcome** for the study!
2. Completed for all infants after randomisation, for every day that the infant is on any form of respiratory support, including oxygen only.
3. **Please ensure the paper copy of the log is correct as this is the source data** – if amended due to discrepancies found during SDV or when completing OC data entry, **all, corrections should be GCP compliant manner**, e.g. changes should be initialled and dated.
4. Paper copy should be kept by the cot side (7-day booklet)
5. An entry should be made every **4 hours**. This can be completed by *any staff member* but will be signed off by delegated staff member at the end of each page.
6. If an infant is recorded as 'Breathing in air' for a full 24 hour period, the Respiratory Support Log can stop being completed. It should be re-started, if further respiratory support becomes necessary. **Do not stop completion of the log as soon as the infant begins to breath in air!!**
7. Data should be entered on OpenClinica; Please do not mark as 'complete' on OpenClincia until infant is discharged home!

Any mistakes noted on the paper Respiratory Support Log should be **edited in a GCP compliant manner, dated, initialled, and explained (if necessary)**
The edit **should not obscure the original entry** (i.e. an audit trail should be maintained);
The original log should be filed in the Data Collection File



SurfON Respiratory Support Log

NPEU OXFORD

Day 1: 20/01/20

Study Number: 10018

Date of birth: 19/01/20

Please complete this log for all infants in the SurfON study after randomisation for every day that the infant is receiving Respiratory support and/or Oxygen

Time Interval	Respiratory Support (please tick ALL that apply)	Oxygen requirement: Did the infant require $FiO_2 \geq 0.45$ to maintain $SaO_2 \geq 92\%$ for a sustained period of ≥ 30 minutes?	Was surfactant administered? (please exclude single dose of surfactant given as study intervention)	Person completing entry (print name)
00:00 to 03:59	Mechanical ventilation ☐ Positive airway pressure (CPAP, BiPAP) ☐ High Flow Therapy ☐ Incubator or low flow oxygen ☐ Breathing in air ☐	Yes ☐ No ☐	Yes ☐ No ☐ *If Yes, please complete Surfactant Form*	Rachel Clark
04:00 to 07:59	Mechanical ventilation ☐ Positive airway pressure (CPAP, BiPAP) ☐ High Flow Therapy ☐ Incubator or low flow oxygen ☐ Breathing in air ☐	Yes ☐ No ☐	Yes ☐ No ☐ *If Yes, please complete Surfactant Form*	Rachel Clark
08:00 to 11:59	Mechanical ventilation ☐ Positive airway pressure (CPAP, BiPAP) ☐ High Flow Therapy ☐ Incubator or low flow oxygen ☐ Breathing in air ☐	Yes ☐ No ☐	Yes ☐ No ☐ *If Yes, please complete Surfactant Form*	Mary Abioye
12:00 to 15:59	Mechanical ventilation ✓ Positive airway pressure (CPAP, BiPAP) ☐ High Flow Therapy ☐ Incubator or low flow oxygen ☐ Breathing in air ☐	Yes ✓ No ☐	Yes ☐ No ✓ *If Yes, please complete Surfactant Form*	Mary Abioye
16:00 to 19:59	Mechanical ventilation ✓ Positive airway pressure (CPAP, BiPAP) ☐ High Flow Therapy ☐ Incubator or low flow oxygen ☐ Breathing in air ☐	Yes ☐ No ✓	Yes ☐ No ✓ *If Yes, please complete Surfactant Form*	Mary Abioye
20:00 to 23:59	Mechanical ventilation ✓ Positive airway pressure (CPAP, BiPAP) ☐ High Flow Therapy ☐ Incubator or low flow oxygen ☐ Breathing in air ☐	Yes ☐ No ✓	Yes ☐ No ✓ *If Yes, please complete Surfactant Form*	Shalini Nair

Sign off by delegated person

I confirm that I have checked the data recorded on this log against the infant's hospital records:

Name: (Print) Rachel Clark Signature: Rachel Clark

Role: Research Nurse Date: 21/01/20

SurfON Respiratory Support Log v1.0, 8-Jun-2020 01865 289 437/738/599 surfon@npeu.ox.ac.uk Sheet 1 of ___

We collect (scanned copy sent via the Upload Tool) first 10 logs from all sites to complete Source Data Verification

Any questions?

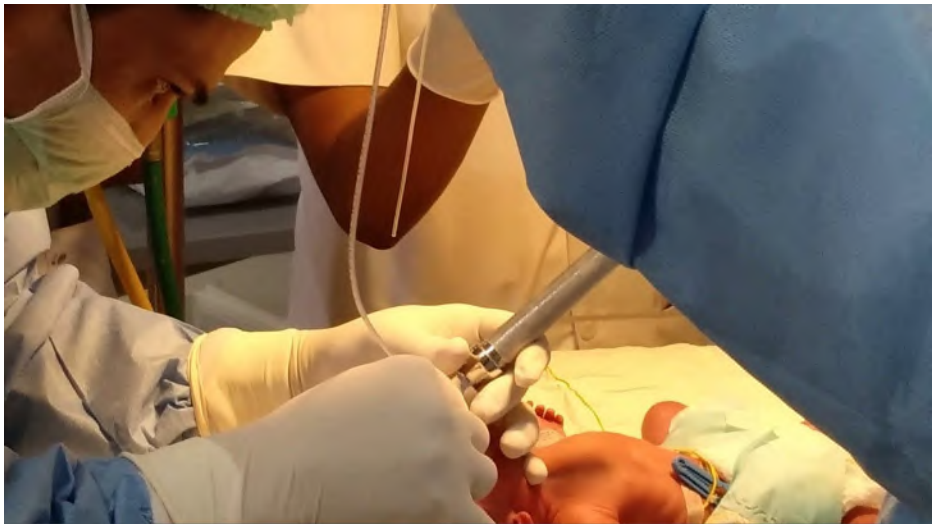
Example of a log that has been completed correctly

Schedule of Trial Procedures

PROCEDURES	BEFORE TRIAL ENTRY	AFTER TRIAL ENTRY				
	Screening	Baseline	Randomisation	Intervention	Data collection	
	Within ≤ 24 hours of birth			Post-randomisation	At hospital discharge	At one year of age
Eligibility assessment	X					
Informed consent		X				
Randomisation			X			
Surfactant administration				X		
Questionnaires		X			X	
Perinatal clinical data collection		X	X	X	X	
Follow-up data collection using routine national database						X
Adverse events assessments (SAEs, SUSARs etc)			X	X	X	

Early Surfactant Therapy group

In order to ensure sufficient separation between the two study groups, it is essential that for infants in the **Early Surfactant Therapy** group, Surfactant is given **as early as possible**, after randomisation.



Any deviation from this guidance should be at the discretion of the attending clinician, following assessment of the infant's clinical condition.

Note: This is not a withdrawal from the study

Expectant Management group

Infants in the **Expectant Management** group should, where possible, be maintained on non-invasive respiratory support alone, at least until a more severe disease threshold is reached, defined as,

sustained (≥ 30 minutes) requirement for $FiO_2 \geq 0.45$ to maintain oxygen saturations (SaO_2) ≥ 92%

Image courtesy: Getty images

This threshold has been determined by clinicians in line with current known variation in clinical practice. It helps ensure sufficient separation between the two study groups. Any deviation from this guidance should be at the discretion of the attending clinician, following assessment of the infant's clinical condition.

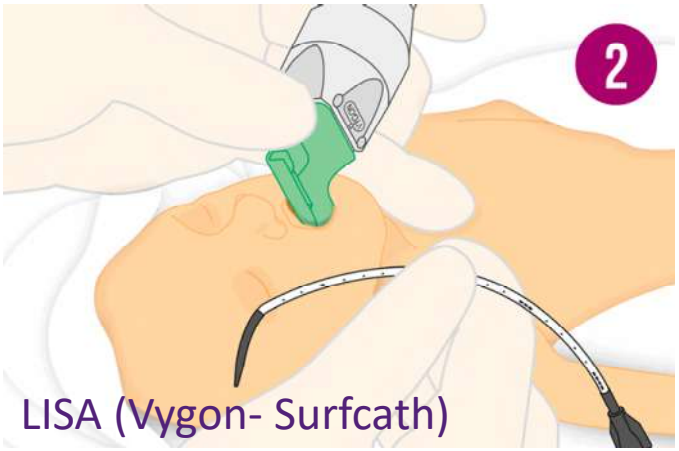
Note: This is not a withdrawal from the study

Surfactant administration

- IMP is CUROSURF®
- Single dose as per the SmPC (100–200 mg/kg (1.25–2.5 ml/kg) in the Protocol
- Dispensed from the hospital stock through routine prescription
- Clinician or advanced nurse practitioner can administer IMP as per local site policy and procedure *(no need to be trained/delegated to work on SurfON as this is standard care)*

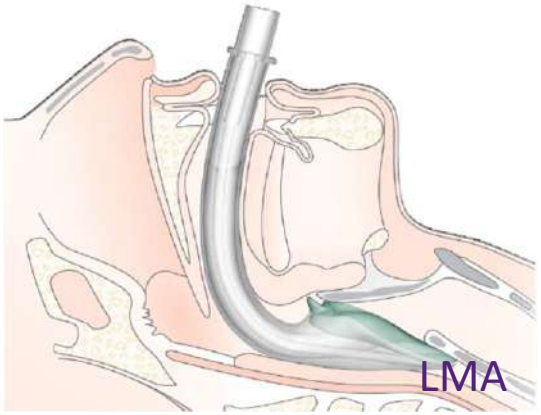
Methods of Surfactant administration

- Surfactant should be administered as per local site policy and procedure (for eg- LISA, INSURE etc); No study-specific requirements



LISA (Vygon- Surfcath)


Medicina Surfactant kit
(VL guided thin cath)


LMA

Data collection

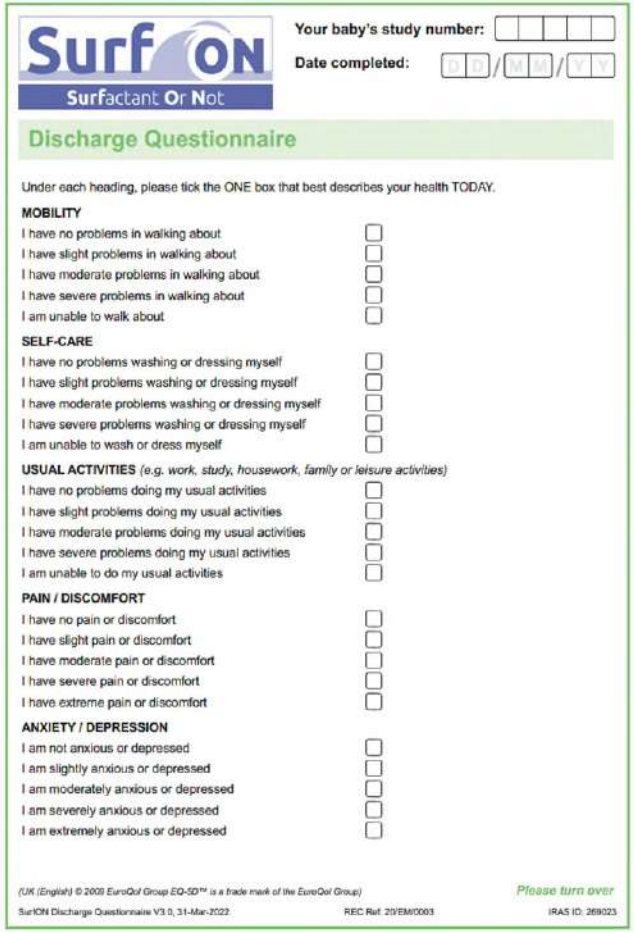
- Primarily using e-CRFs on *Openclinica*
- **Trial Intervention Form** is completed for all infants, regardless of which study arm they are randomised to.
- Important to maintain **Respiratory Support Log** once infant has been randomised to either trial groups (primary outcome)
- Further details on data collection will be discussed in Part II – Data Management

Schedule of Trial Procedures

PROCEDURES	BEFORE TRIAL ENTRY	AFTER TRIAL ENTRY				
	Screening	Baseline	Randomisation	Intervention	Data collection	
	Within ≤ 24 hours of birth			Post-randomisation	At hospital discharge	At one year of age
Eligibility assessment	X					
Informed consent		X				
Randomisation			X			
Surfactant administration				X		
Questionnaires		X			X	
Perinatal clinical data collection		X	X	X	X	
Follow-up data collection using routine national database						X
Adverse events assessments (SAEs, SUSARs etc)			X	X	X	

Administer Trial Discharge Questionnaire

V4.0 31st Mar 2022



*SurfON Stickers to act as reminders (or) add a reminder note on electronic notes!

- ✓ Administer when the ***'infant'*** is discharged home remembering to enter onto OpenClinica – file in the Data Collection File
- ✓ **Outcomes Form** completed on OpenClinica

Schedule of Trial Procedures

PROCEDURES	BEFORE TRIAL ENTRY	AFTER TRIAL ENTRY				
	Screening	Baseline	Randomisation	Intervention	Data collection	
	Within ≤ 24 hours of birth			Post-randomisation	At hospital discharge	At one year of age
Eligibility assessment	X					
Informed consent		X				
Randomisation			X			
Surfactant administration				X		
Questionnaires		X			X	
Perinatal clinical data collection		X	X	X	X	
Follow-up data collection using routine national database						X
Adverse events assessments (SAEs, SUSARs etc)			X	X	X	

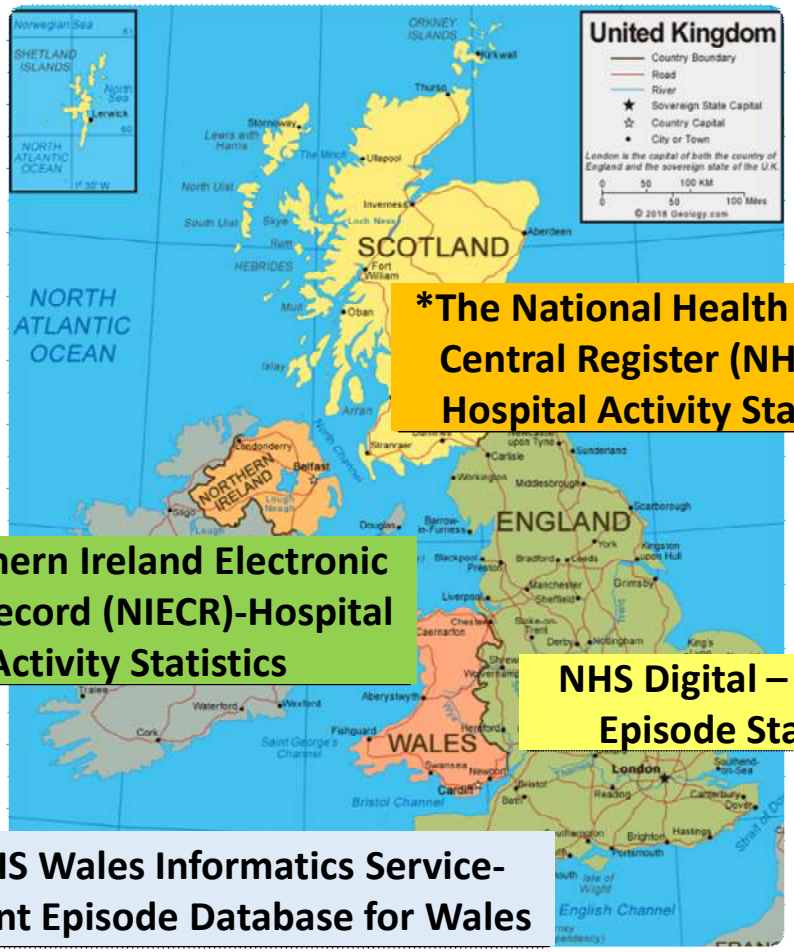
Remote follow up – Health Economics

-Follow up to occur between infant discharge home and **one year of age**, corrected for prematurity

-Paediatric secondary care use and associated costs

-Using routine national databases

- No direct contact with participants



***The National Health Service Central Register (NHSCR) - Hospital Activity Statistics**

***Northern Ireland Electronic Care Record (NIECR)-Hospital Activity Statistics**

NHS Digital – Hospital Episode Statistics

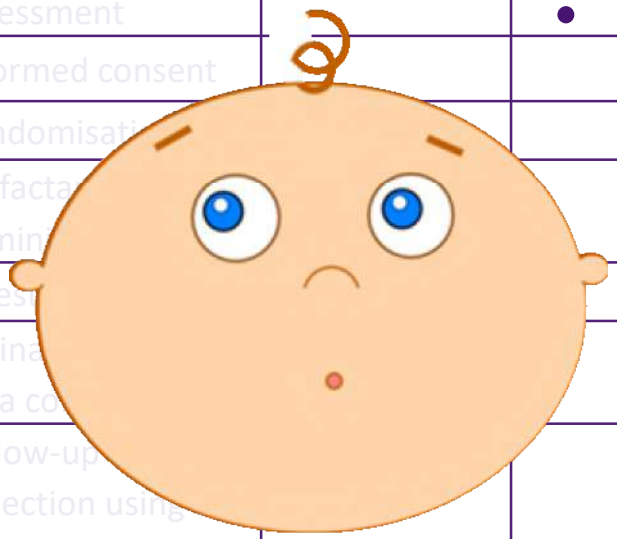
***NHS Wales Informatics Service- Patient Episode Database for Wales**

**databases to be confirmed*

Schedule of Trial Procedures

PROCEDURES	BEFORE TRIAL ENTRY	AFTER TRIAL ENTRY				
	Screening	Baseline				tion
	Within ≤ 24 h					one of age
Eligibility assessment	X					
Informed consent		X				
Randomisati			X			
Surfacta admin				X		
Ques		X			X	
Perina data co		X	X	X	X	
Follow-up collection using routine national database						X
Adverse events assessments (SAEs, SUSARs etc)			X	X	X	

Any Questions?



Withdrawals

- Need for additional respiratory intervention for infants in the Expectant Management group (or) decision to not administer surfactant in the Early Surfactant Therapy group *does not constitute* to withdrawal
- Right to withdraw from the study at any time, however, data collected up until the point of withdrawal will be retained (GDPR). Withdrawals can also occur because of other reasons
- Document withdrawal in medical notes; Ask for permission to continue with data collection from infant's and mother's medical notes and also remote follow up
- Check whether parents would like to receive study results
- **Withdrawal Form** is completed on Openclinica

Surf ON
Surfactant Or Not

PART I – Study Overview & Procedures

Safety Reporting & Hospital Transfers

Adverse Event (AE)

- Any untoward medical occurrence in a participant to whom an investigational intervention has been administered, including occurrences which are not necessarily caused by or related to that intervention

Serious Adverse Event (SAE)

- Any adverse event that:
  - Results in death
  - Is life-threatening
  - Requires inpatient hospitalisation or prolongation of existing hospitalisation
  - Results in persistent or significant disability/incapacity
  - Is a congenital anomaly/birth defect
  - *Other important medical events*

SAEs for reporting

- Any occurrences that fit the definition of an SAE

  In particular, the following events will need to be reported:

- Death
- Transfer to another hospital related to early respiratory management
  - for escalation of care
  - for neonatal intensive care because of lack of intensive care cot capacity in the NICU or LNU of birth

  (Please note that transfers for a lower level of care (SCU) or for reasons unrelated to respiratory management do *not* need to be reported as an SAE)
- Serious complication of ETT intubation such as hypoxia resulting in encephalopathy
- Severe pulmonary haemorrhage
- Severe intracranial haemorrhage

SAE reporting

- The Principal Investigator (PI) and site study team have responsibility for safety reporting at their site. They must inform SurfON Study Team of all SAEs that occur, and of other relevant safety issues
- Any member of the team can report SAEs, however *do not wait for the causality assessment* to be completed

- SAEs must be reported ***as soon as possible and within 24 hours of the site becoming aware of it***
- SAEs should be reported from randomisation up until infant's discharge home

- SAEs can be reported by phone, email or online
- In the case of out-of-hours reporting, please phone 0800 1385 451.

Internal Use Only
SAE Identifier: _____

Serious Adverse Event Report Form (CTIMP)

SurfON

Form completion instructions overleaf

1. **Report type** *(tick one)* Initial report ☐ Follow-up information ☐

2. **Site name:** _____

3. **Participant details**

Study number ☐☐☐☐☐

Participants initials: ☐☐☐

Date of birth ☐☐/☐☐/☐☐

Report using SAE Report Form

4. **ADVERSE EVENT DESCRIPTION:**

(Please record diagnosis if known, an account of the event including signs and symptoms if diagnosis not known, any interventions given to manage the event including dates for these and if event fatal, cause of death if known):

_____

_____

_____

_____

_____

_____

5. **Start date and time of SAE:** ☐☐/☐☐/☐☐ ☐☐:☐☐

6. **Stop date and time of SAE:** ☐☐/☐☐/☐☐ ☐☐:☐☐ Or ongoing ☐

7. **Date and time site became aware of SAE:** ☐☐/☐☐/☐☐ ☐☐:☐☐

Please complete and send this form immediately, no later than 24 hours after becoming aware of the SAE.

PLEASE FAX/EMAIL FORM TO: Trial Co-ordinating Centre
+44 (0)1865 289740 ouh-tr.surfon@nhs.net; surfon@npeu.ox.ac.uk

Internal Use Only
SAE Identifier: _____

Study number: ☐☐☐☐☐

SurfON

Serious Adverse Event Report Form

Form completion instructions overleaf

8. **Please record severity of event:** *(tick one box only)*

Mild ☐ Moderate ☐ Severe ☐

9. **Reason this event is classified as Serious:** *(tick one box only)*

Fatal ☐ Life threatening ☐
Requiring/prolonging hospitalisation ☐ Congenital anomaly/birth defect ☐
Significant disability/incapacity ☐ Other important medical event ☐

10. **Relevant medical history:** *(including co-existing medical conditions, allergies or similar experiences)*

_____

_____

_____

_____

11. **Laboratory results relevant to the SAE:**

_____

_____

_____

_____

12. **Specify the study drug details below:**

Study drug name	Dose	Frequency	Route	Date started	If discontinued, date stopped
				D D/M M/Y Y	D D/M M/Y Y
				D D/M M/Y Y	D D/M M/Y Y

Did the event resolve after stopping study drug? Yes ☐ No ☐ N/A ☐

Did the event reappear after reintroduction? Yes ☐ No ☐ N/A ☐

Action taken with study drug: None ☐ Discontinued temporarily ☐
Dose reduced ☐ Discontinued ☐
Dose temporarily reduced ☐

SAE Report Form on OpenClinica – Initial Report

SF_10001: Serious Adverse Event Report Form

1. Report type	SAE number	Form number (for this SAE)
If this is the first time the SAE has been reported, please select "Initial report". If you are submitting new, updated or corrected information for a previously reported SAE, please select "Follow-up information".	*If this CRF relates to the patient's first SAE, enter 1. If the patient has had more than one SAE, please record the SAE number that this applies to*	*If this is the initial report, enter 1. If this is a follow-up form, please record the number of CRFs you have attempted to complete for this SAE, including this one*
(•) Initial report ( ) Follow-up information	1	1

2. Site

Site name
Leicester Royal Infirmary

3. Participant details

DOB on Entry Form: 2020-09-25	
Date of birth 2020-09-25	
Sex ( ) Male (•) Female ( ) Indeterminate	
Enter participant's last known weight either in grams OR kilograms	
Weight in grams *(g)* 3835	**Weight in kilograms** *(kg)* 3.835

SAEs that do not need reporting

- Pulmonary air leaks (pneumothoraces or pneumomediastinum)
- Late onset sepsis
- Need for mechanical ventilation via an ETT
- Extra-Corporeal Membrane Oxygenation (ECMO)
- Inhaled Nitric Oxide (iNO)

*These are **pre-defined study outcomes** in the study population and as such will only be recorded on the case report forms but not expeditiously reported*

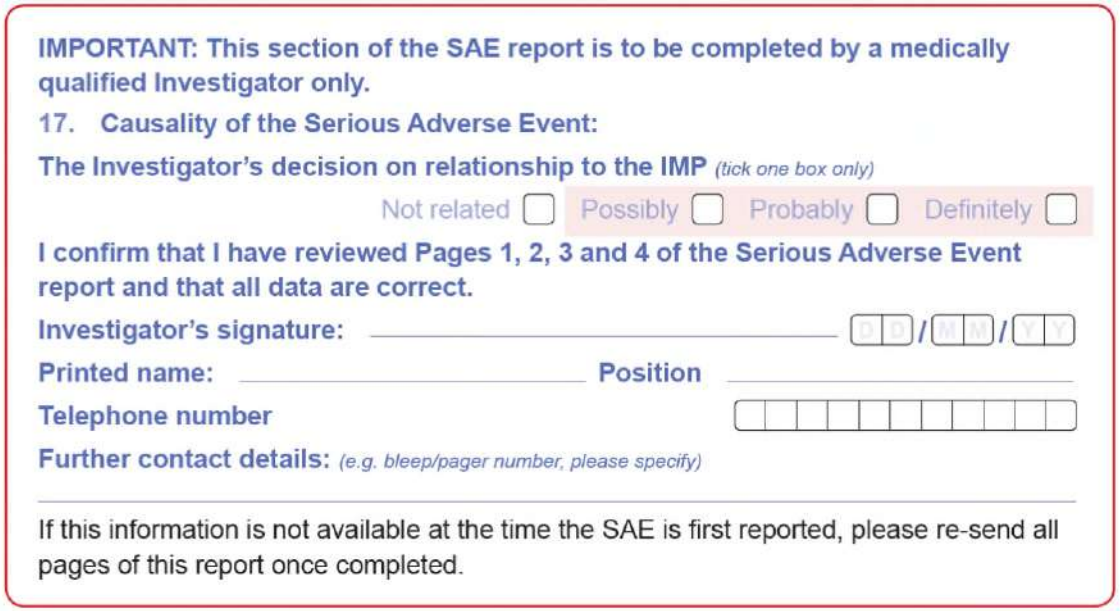
- Common minor deviations from normal haematological values, including anaemia and thrombocytopenia
- Common minor deviations from normal biochemical values including hyponatraemia, hyperbilirubinaemia, and hypoglycaemia
- Patent ductus arteriosus

*These are **foreseeable occurrences** in this population of infants and as such do not require reporting as SAEs*

SAE causality assessment

✓ Any member of the team can report SAEs, however causality assessment (question 17) should be done by delegated members of the team (recorded on **delegation log**).

-We recommend **more than one** person is delegated to complete causality assessment to cover any absences



IMPORTANT: This section of the SAE report is to be completed by a medically qualified Investigator only.

17. Causality of the Serious Adverse Event:

The Investigator's decision on relationship to the IMP *(tick one box only)*

Not related ☐ Possibly ☐ Probably ☐ Definitely ☐

I confirm that I have reviewed Pages 1, 2, 3 and 4 of the Serious Adverse Event report and that all data are correct.

Investigator's signature: _____ D D / M M / Y Y

Printed name: _____ **Position** _____

Telephone number ☐☐☐☐☐☐☐☐☐☐☐

Further contact details: *(e.g. bleep/pager number, please specify)*

If this information is not available at the time the SAE is first reported, please re-send all pages of this report once completed.

-If a suitable person is not available, DO NOT WAIT FOR THIS ASSESSMENT TO REPORT THE SAE*.* Complete the form and send to SurfON Study Team **asap** without this information, and complete the causality assessment section as soon as possible.

Surf ON
Surfactant Or Not

Curosurf

Summary of Product Characteristics Updated 28-Jun-2018 | Chiesi Limited

1. Name of the medicinal product

CUROSURF® 120mg / vial Endotracheopulmonary Instillation Suspension

CUROSURF® 240mg / vial Endotracheopulmonary Instillation Suspension

2. Qualitative and quantitative composition

One 1.5 ml vial contains 120mg of phospholipid fraction from porcine lung (poractant alfa).

One 3.0ml vial contains 240mg of phospholipid fraction from porcine lung (poractant alfa).

Composition per ml of suspension: phospholipid fraction from porcine lung 80mg/ml, equivalent to about 74mg/ml of total phospholipids and 0.9mg/ml of low molecular weight hydrophobic proteins.

CUROSURF is a natural surfactant, prepared from porcine lungs, containing almost exclusively polar lipids, in particular phosphatidylcholine (about 70% of the total phospholipid content), and about 1% of specific low molecular weight hydrophobic proteins SP-B and SP-C.

For the full list of excipients, see section 6.1.

3. Pharmaceutical form

Endotracheopulmonary instillation suspension

A white to yellow sterile suspension for endotracheopulmonary instillation in single dose vials.

4. Clinical particulars

4.1 Therapeutic indications

For the treatment, including early rescue of Respiratory Distress Syndrome (RDS) or hyaline membrane disease in newborn babies.

Prophylactic use in premature infants requiring intubation for stabilisation at risk from RDS or with evidence of surfactant deficiency.

4.2 Posology and method of administration

4.2.1 Posology

) (1.25-2.5ml/kg), administered in a single dose as soon as possible

t about 12-hourly intervals, may also be administered if RDS is rating respiratory status of the infants (maximum total dose of 300-

nistered as soon as possible after birth (preferably within 15 minutes). ours after the first dose and then 12 hours later in babies who have endent (maximum total dose of 300 to 400mg/kg).

e trained and experienced in the care, resuscitation and stabilisation of he endotracheopulmonary route in infants whose heart rate and are being continuously monitored as it is usually feasible in neonatal

should be stored in a refrigerator at +2°C to +8°C. The vial should be mple by holding it in the hand for a few minutes, and gently turned r to obtain a uniform suspension.

l using a sterile needle and syringe following the instruction described hen be used to instil CUROSURF into the lungs.

CUROSURF can be administered either by:

a. Disconnecting the baby from the ventilator

Disconnect the baby momentarily from the ventilator and administer 1.25 to 2.5ml/kg of the suspension, as a single bolus, directly into the lower trachea via the endotracheal tube. Perform approximately one minute of hand-bagging and

For SurfON, the assessor must refer to the latest approved **SmPC as per SurfON Protocol (28 June 2018)** in order to assess expectedness.

If the SAE is related to the IMP and the event is unexpected (i.e. is not consistent with SmPC) then this is a SUSAR.

SAE – Follow up information

- ✓ On receipt of new relevant or missing information, site staff can either use the previously reported form to send the information (or) use a new SAE report form

- ✓ If using previously reported form, new information should be added in a **GCP compliant** manner
  - For eg, if adding new information, it should be made clear *who* has added the information and *when* it was added by signing *initials and date* next to each of the new entries made; If adding minimal data, for eg, end date, this could be added to existing SAE report form; Extensive information should be on new SAE form.

- ✓ This is applicable to both electronic (OpenClinica) or paper reporting form

SAE Report Form on OpenClinica - Follow up Information

SF_10002: Serious Adverse Event Report Form

1. Report type
If this is the first time the SAE has been reported, please select "Initial report". If you are submitting new, updated or corrected information for a previously reported SAE, please select "Follow-up information".

○ Initial report ◉ Follow-up information

SAE number
If this CRF relates to the patient's first SAE, enter 1. If the patient has had more than one SAE, please record the SAE number that this applies to

1

Form number (for this SAE)
If this is the initial report, enter 1. If this is a follow-up form, please record the number of CRFs you have attempted to complete for this SAE, including this one

3

2. Site

Site name

Luton & Dunstable University Hospital

3. Participant details

DOB on Entry Form: 2022-02-03

Date of birth

2022-02-03

Sex

○ Male ◉ Female ○ Indeterminate

Enter participant's last known weight either in grams OR kilograms

Weight in grams
(g)

Weight in kilograms
(kg)

5.45

✓Follow up information should be provided until the SAE is resolved (although further follow up information may be still be provided after this)

Incident Reporting

Incidents & Breaches

- **What is an incident?** It can be defined as a deviation from:
  - Protocol
  - Trial procedures
  - Good Clinical Practice
  - Regulatory requirements

1. Parent consented by someone not on the delegation log
2. Old version of a form used

Incidents and protocol deviations will be defined as a **serious breach** if the incident is likely to affect to a significant degree either:

- The safety, physical or mental integrity of the subjects of the trial
- The scientific value of the trial

Incident and Deviation Reporting Form

Site Name _____

Principal Investigator: _____

Participant Study Number (if applicable): ☐☐☐☐☐☐☐☐

Participant day and month of date of birth (if applicable): ☐☐/☐☐

Incident number: *(to be completed by NPEU CTU)* ☐☐☐☐☐☐☐☐

Date incident occurred (started): ☐☐/☐☐/☐☐

Detail of incident: _____

Resolution: *(Include actual and planned corrective and preventative action at site)*

If this information is not available at the time the incident is first reported, please send without this information and send this information later.

Details of Reporter:

Name: _____

Role: _____

Signature: _____ Date: ☐☐/☐☐/☐☐

List any relevant documentation included with this form:

_____

_____

_____

_____

Please complete and send immediately after becoming aware of the incident.

One copy to NPEU CTU, along with relevant documentation, and one to be filed in the Investigator Site File.

Report these as soon as possible using **Incident and Deviation Form**

Email: ouh-tr.surfon@nhs.net; surfon@npeu.ox.ac.uk

Fax: +44 (0)1865 289740

NPEU CTU Receipt:

Received at NPEU CTU by:

Name: _____

Role: _____

Signature: _____ Date: ☐☐/☐☐/☐☐

NPEU CTU comments to reporting site:

_____

_____

_____

Name: _____

Role: _____

Signature: _____ Date: ☐☐/☐☐/☐☐

Incident Reporting

- Only Paper CRF available; Kept in the Site Documents Box
- **Email**: Any incidents containing personal identifiable information should be uploaded **NPEU CTU Upload Tool**
- **Phone**: **01865** 289 437/ 738 (or) 617 965 (office hours)
- Keep one copy in the **Investigator Site File**

Surf ON
Surfactant Or Not

Data collection – in the case of **Hospital Transfers**

What to do in the case of **Hospital Transfers?**

- ✓ Notify the SurfON Study Team of ***any*** transfer as soon as it is considered; Internal transfers that could occur, for example, transfer from NNU to surgical ward within the same hospital site is not considered to be a hospital transfer.

- ✓ However, if the transfer occurs between different hospital sites under the same trust (example – between Royal Derby and Burton hospital under University Hospitals of Derby and Burton NHS Foundation Trust), please complete the **Transfer Form** in OpenClinica & **Transfer Pack** should be provided along with the infant; *No additional approvals are needed* to complete data collection as the REC approval is provided overall to the trust (to act as a recruiting site) under the PI. Responsibilities as the recruiting site will apply.

- ✓ If the transfer occurs between different hospital sites under different trusts (example – between Royal Derby hospital under University Hospitals of Derby and Burton NHS Foundation Trust to Evelina Hospital under Guy's and St Thomas' NHS Foundation Trust), please complete the **Transfer Form** in OpenClinica & **Transfer Pack** should be provided along with the infant; *Additional approvals will be needed for the transferred site to act as a Continuing Care Site.* Study activities (e.g. administration of the intervention), data collection can only be carried out at sites that have the necessary approvals. It is to be noted that recruiting site is still responsible for collecting data and entering it on OpenClinica.

Notify the SurfON Study Team of any transfer as soon as it is considered

Data Collection – in the case of **Hospital Transfers**

SurfON Participant Transfer Pack

SurfON
Surfactant Or Not

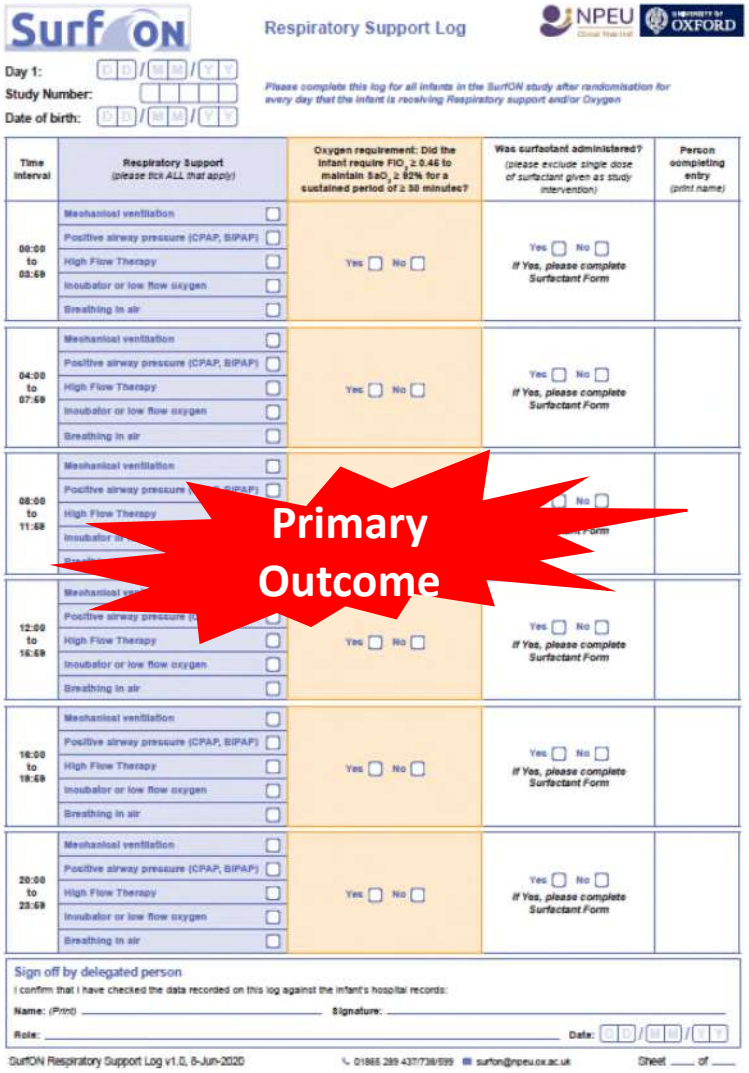
Study number: ☐☐☐☐☐☐ **Infant Randomised to: Early Surfactant Therapy** ☐ **OR Expectant Management** ☐

Participant Transfer Pack Contents
SurfON sticker (for use on infant's medical notes) & SurfON cot card
Mother's Discharge Questionnaire (if the mother has not provided consent to complete the questionnaire please remove it from the transfer pack)
SurfON Respiratory Support Log
SurfON Incident and Deviation Form
SurfON Serious Adverse Event (SAE) Report Form
SurfON Surfactant Form
SurfON Transfer Form
SurfON Withdrawal Form
SurfON Guidance Sheet for Continuing Care Sites
SurfON Guidance Sheets 5, 6 & 8
Freepost envelope for Coordinating Centre

SurfON Study team
NPEU CTU
Nuffield Department of Population Health
University of Oxford, Old Road Campus
Headington, Oxford, OX3 7LF
Tel: 01865 289 437 / 738 / 599
Fax: 01865 289 740
Email: surfon@npeu.ox.ac.uk

Documents to be added to envelope by site at time of transfer
Recruiting site PIL
Photocopy of existing Respiratory Support Log

Data Collection – in the case of **Hospital Transfers**


SurfON Respiratory Support Log

NPEU OXFORD

Day 1: D D / M M / Y Y

Study Number:

Date of birth: D D / M M / Y Y

Please complete this log for all infants in the SurfON study after randomisation for every day that the infant is receiving Respiratory support and/or Oxygen

Time Interval	Respiratory Support (please tick ALL that apply)	Oxygen requirement: Did the infant require $FIO_2 \geq 0.46$ to maintain $SaO_2 \geq 92\%$ for a sustained period of ≥ 30 minutes?	Was surfactant administered? (please exclude single dose of surfactant given as study intervention)	Person completing entry (print name)
00:00 to 03:59	Mechanical ventilation ☐ Positive airway pressure (CPAP, BiPAP) ☐ High Flow Therapy ☐ Incubator or low flow oxygen ☐ Breathing in air ☐	Yes ☐ No ☐	Yes ☐ No ☐ *If Yes, please complete Surfactant Form*	
04:00 to 07:59	Mechanical ventilation ☐ Positive airway pressure (CPAP, BiPAP) ☐ High Flow Therapy ☐ Incubator or low flow oxygen ☐ Breathing in air ☐	Yes ☐ No ☐	Yes ☐ No ☐ *If Yes, please complete Surfactant Form*	
08:00 to 11:59	Mechanical ventilation ☐ Positive airway pressure ☐ High Flow Therapy ☐ Incubator or low flow oxygen ☐ Breathing in air ☐	Yes ☐ No ☐	Yes ☐ No ☐ *If Yes, please complete Surfactant Form*	
12:00 to 15:59	Mechanical ventilation ☐ Positive airway pressure ☐ High Flow Therapy ☐ Incubator or low flow oxygen ☐ Breathing in air ☐	Yes ☐ No ☐	Yes ☐ No ☐ *If Yes, please complete Surfactant Form*	
16:00 to 19:59	Mechanical ventilation ☐ Positive airway pressure (CPAP, BiPAP) ☐ High Flow Therapy ☐ Incubator or low flow oxygen ☐ Breathing in air ☐	Yes ☐ No ☐	Yes ☐ No ☐ *If Yes, please complete Surfactant Form*	
20:00 to 23:59	Mechanical ventilation ☐ Positive airway pressure (CPAP, BiPAP) ☐ High Flow Therapy ☐ Incubator or low flow oxygen ☐ Breathing in air ☐	Yes ☐ No ☐	Yes ☐ No ☐ *If Yes, please complete Surfactant Form*	

Primary Outcome

Sign off by delegated person

I confirm that I have checked the data recorded on this log against the infant's hospital records:

Name: (Print) _____ Signature: _____

Role: _____ Date: D D / M M / Y Y

SurfON Respiratory Support Log v1.0, 8-Jun-2020 ✆ 01865 289 437/738/599 ✉ surfon@npeu.ox.ac.uk Sheet ___ of ___

SurfON Cot card

SurfON Randomised Sticker

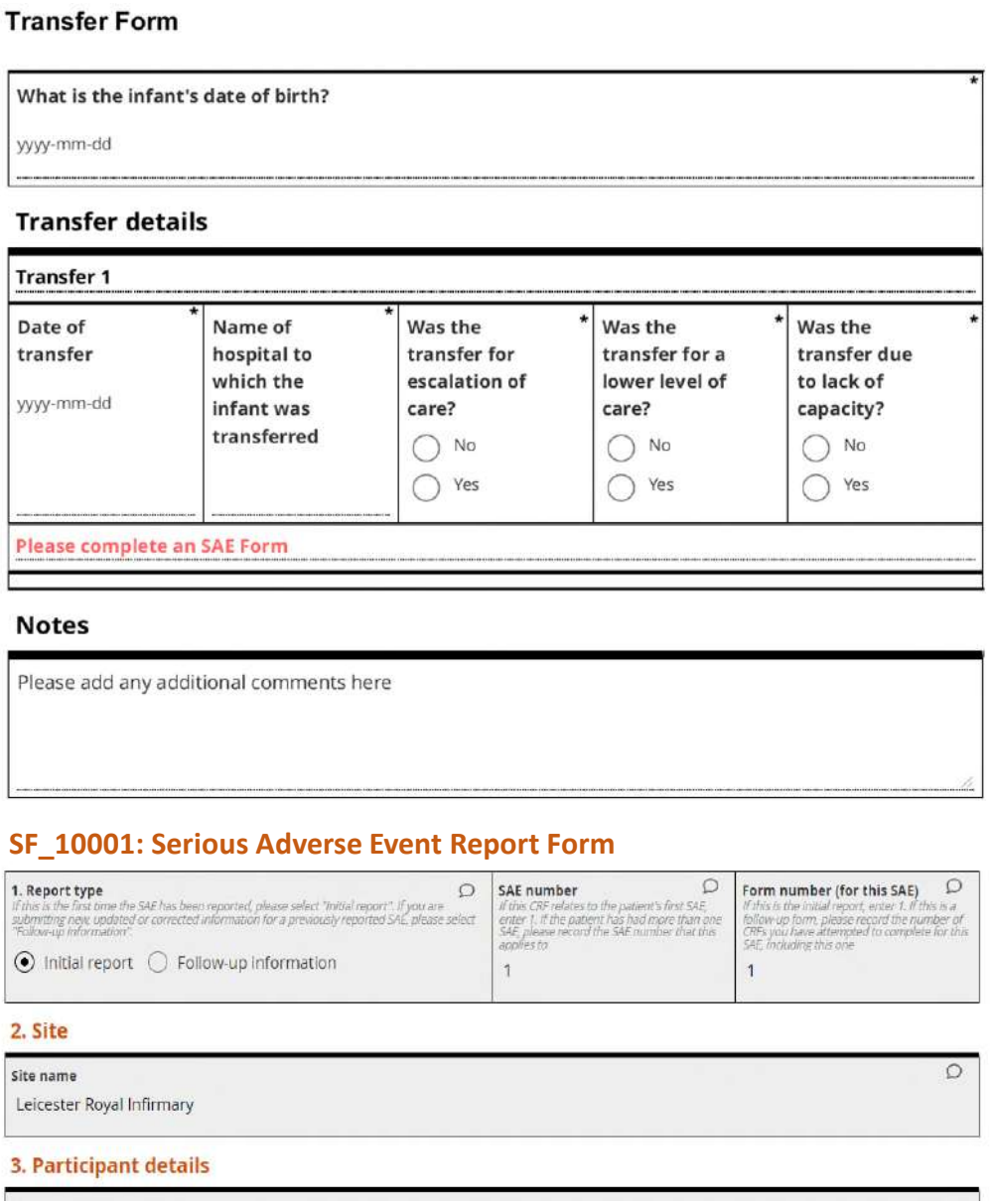
SurfON Discharge Questionnaire Sticker

Important Note: Recruiting Site is **responsible for collecting all data** related to the participant and entering it on OpenClinica

When does a **Hospital Transfer** become a **SAE?**

- ✓ If the transfer to another hospital is related to early respiratory management
  - for escalation of care
  - for neonatal intensive care because of lack of intensive care cot capacity in the NICU or LNU of birth
- it must also be reported as a **Serious Adverse Event** (along with completion of **Transfer Form** on OpenClinica & provision of **Transfer Pack** with the infant)

✓ *Please note that transfers for a lower level of care (SCU) or for reasons unrelated to respiratory management do not need to be reported as an SAE*



Transfer Form

What is the infant's date of birth? *

yyyy-mm-dd

Transfer details

Transfer 1

Date of transfer *	Name of hospital to which the infant was transferred *	Was the transfer for escalation of care? *	Was the transfer for a lower level of care? *	Was the transfer due to lack of capacity? *
yyyy-mm-dd		○ No ○ Yes	○ No ○ Yes	○ No ○ Yes

Please complete an SAE Form

Notes

Please add any additional comments here

SF_10001: Serious Adverse Event Report Form

1. Report type	SAE number	Form number (for this SAE)
If this is the first time the SAE has been reported, please select "Initial report". If you are submitting new, updated or corrected information for a previously reported SAE, please select "Follow-up information". ● Initial report ○ Follow-up information	If this CRF relates to the patient's first SAE, enter 1. If the patient has had more than one SAE, please record the SAE number that this applies to: 1	If this is the initial report, enter 1. If this is a follow-up form, please record the number of CRFs you have attempted to complete for this SAE, including this one: 1

2. Site

Site name: Leicester Royal Infirmary

3. Participant details

THE END OF PART 1

PART II - Data Management

Part II - Presentation overview

- **DATA MANAGEMENT**
  - Case Report Forms
  - How data is collected throughout the trial period
  - Completing Screening Logs online
  - Study database –Openclinica

- **MONITORING & ARCHIVING**

Case Report Forms (CRFs)

OpenClinica
Open Source for Clinical Research

Electronic CRFs

SurfON
Demonstration version only
Randomisation Program

Web-based 24 hour service

Paper CRF

Other modes of reporting

Telephone

Email

Description of the CRFs

SurfON CRFs	
SurfON Randomisation Form	
SurfON Contact Details Form	
SurfON Trial Entry Form	OpenClinica
SurfON Trial Intervention Form	OpenClinica
SurfON Respiratory Support Log	OpenClinica
SurfON Surfactant Form	OpenClinica
SurfON Outcomes Form	OpenClinica
SurfON Transfer Form	OpenClinica
SurfON Withdrawal Form	OpenClinica
SurfON SAE Report Form	OpenClinica
SurfON Incident and Deviation Form	

Paper copy kept near infant's cot side

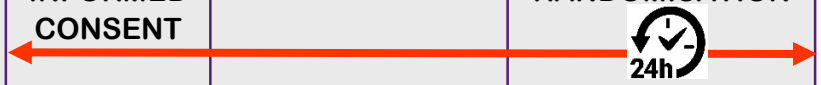
Reported online, by phone or by email

Key:

Paper CRFs available

OpenClinica *e-CRFs available*

Data Collection Overview

Before trial entry	DATA COLLECTION		
SCREENING & ELIGIBILITY ASSESSMENT	**INFORMED CONSENT**	**BASELINE**	**RANDOMISATION** 
PIL to parent Complete Screening Log (randomisation system)	Complete Consent form	Provide Trial Entry Questionnaire to mother 	Randomisation form (randomisation system)
		Provide Thank You Card	Contact details form (randomisation system)
		Use Cot Card & SurfON Stickers	Trial Entry form 

Data Collection Overview

Before trial entry	DATA COLLECTION					
SCREENING & ELIGIBILITY ASSESSMENT	**INFORMED CONSENT**	**BASELINE**	**RANDOMISATION** 	**INTERVENTION**	**AT INFANT'S HOSPITAL DISCHARGE**	**REMOTE FOLLOW UP**
PIL to parent Complete Screening Log (randomisation system)	Complete Consent form	Provide Trial Entry Questionnaire to mother 	Randomisation form (randomisation system)	Trial Intervention form* OpenClinica	Provide Discharge Questionnaire to mother 	At one year of age, corrected for prematurity SurfON Study Team conducts data collection using routine national databases with no direct contact with participants
		Provide Thank You Card	Contact details form (randomisation system)	Respiratory Support Log*  OpenClinica 	Outcomes form OpenClinica	
		Use Cot Card & SurfON Stickers	Trial Entry form OpenClinica			

Note– *to complete for all infants regardless of which group they are randomised to

Data Collection Overview

Before trial entry	DATA COLLECTION					
SCREENING & ELIGIBILITY ASSESSMENT	**INFORMED CONSENT**	**BASELINE**	**RANDOMISATION** (24h)	**INTERVENTION**	**AT INFANT'S HOSPITAL DISCHARGE**	**REMOTE FOLLOW UP**
PIL to parent Complete Screening Log (randomisation system)	Complete Consent form	Provide Trial entry Questionnaire to mother	Randomisation form (randomisation system)	Trial Intervention form* OpenClinica	Provide Discharge Questionnaire to mother	At one year of age, corrected for prematurity SurfON Study Team conducts data collection using routine national databases with no direct contact with participants
		Provide Thank You Card	Contact details form (randomisation system)	Respiratory Support Log* OpenClinica	Outcomes form OpenClinica	
		Use Cot Card & SurfON Stickers	Trial entry form OpenClinica	Important		

Surfactant form	Transfer Form	Withdrawal Form	SAE Report Form	Incident and Deviation Form
OpenClinica	OpenClinica	OpenClinica	OpenClinica	

Note– *to complete for all infants regardless of which group they are randomised to

SurfON

Eligibility/Screening Log

Please ensure that a summary of monthly screening data is completed online at: https://rct.npeu.ox.ac.uk/surfon

Full Title:	Multicentre, open-label, randomised controlled trial of early surfactant therapy versus expectant management in late preterm and early term infants with respiratory distress.		IRAS ID: 269023 REC Ref: 20/EM/0003 EudraCT no: 2019-003764-45
Chief Investigator:	Professor Elaine M Boyle		
Site Name:		**Principal Investigator:**	

Patient			Randomised			
Local ID number	Date assessed for eligibility DD/MM/YY	Corrected gestational age in weeks	Eligible for SurfON?	Randomised to SurfON?	Study ID	If NOT randomised please give reason If other, please specify
	/ /		Y ☐ N ☐	Y ☐ N ☐		Parent(s) declined ☐ Clinical Decision ☐ Staff unavailable ☐ Other ☐ *If Other, specify*
	/ /		Y ☐ N ☐	Y ☐ N ☐		Parent(s) declined ☐ Clinical Decision ☐ Staff unavailable ☐ Other ☐ *If Other, specify*

Important: Screening logs must be completed online on the Randomisation website on a monthly basis ! **Centre log-in** provided and not individual user log-in

https://rct.npeu.ox.ac.uk/surfon/login.php

	/ /		Y ☐ N ☐	Y ☐ N ☐		*If Other, specify*
	/ /		Y ☐ N ☐	Y ☐ N ☐		Parent(s) declined ☐ Clinical Decision ☐ Staff unavailable ☐ Other ☐ *If Other, specify*
	/ /		Y ☐ N ☐	Y ☐ N ☐		Parent(s) declined ☐ Clinical Decision ☐ Staff unavailable ☐ Other ☐ *If Other, specify*
	/ /		Y ☐ N ☐	Y ☐ N ☐		Parent(s) declined ☐ Clinical Decision ☐ ... her ☐ *If Other, specify*
						...ent(s) declined ☐ ... ...ther ☐ ...ther, specify
						...ent(s) declined ☐ Cl... ... unavailable ☐ Other ☐ ...ther, specify

Paper Screening Log is for internal use only (need not be submitted to SurfON study team)

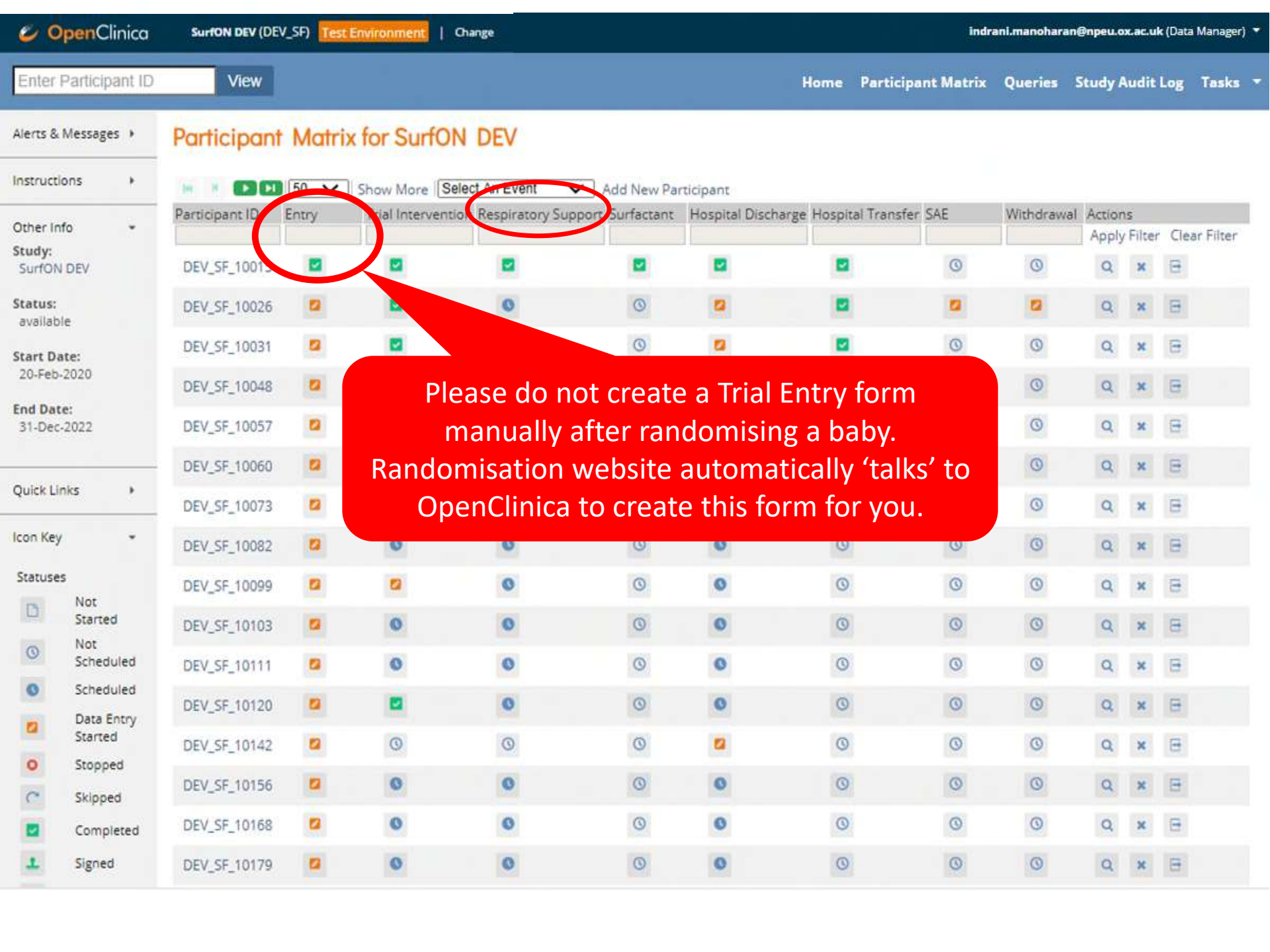
FOR INTERNAL USE ONLY

NPEU Clinical Trials Unit
UNIVERSITY OF OXFORD

Surf ON
Surfactant Or Not

OpenClinica
Open Source for Clinical Research

- Data entry on OpenClinica can be completed only by trained & delegated staff
- Individual user log-in details will be given after training; Data queries & resolving them will be covered in the training (Note: Training log demonstrating training completion must be submitted to surfon@npeu.ox.ac.uk before log-in details can be provided)
- Training materials will be available to access from SurfON website (https://www.youtube.com/watch?v=tuCt48MUNDI)


OpenClinica
SurfON DEV (DEV_SF) Test Environment | Change
indrani.manoharan@npeu.ox.ac.uk (Data Manager)
Enter Participant ID
View
Home
Participant Matrix
Queries
Study Audit Log
Tasks
Alerts & Messages
Instructions
Other Info
Study:
SurfON DEV
Status:
available
Start Date:
20-Feb-2020
End Date:
31-Dec-2022
Quick Links
Icon Key
Statuses
Not Started
Not Scheduled
Scheduled
Data Entry Started
Stopped
Skipped
Completed
Signed
Participant Matrix for SurfON DEV
Show More
Select An Event
Add New Participant
Participant ID
Entry
Respiratory Support
Surfactant
Hospital Discharge
Hospital Transfer
SAE
Withdrawal
Actions
Apply Filter
Clear Filter
DEV_SF_10026
DEV_SF_10031
DEV_SF_10048
DEV_SF_10057
DEV_SF_10060
DEV_SF_10073
DEV_SF_10082
DEV_SF_10099
DEV_SF_10103
DEV_SF_10111
DEV_SF_10120
DEV_SF_10142
DEV_SF_10156
DEV_SF_10168
DEV_SF_10179
Please do not create a Trial Entry form manually after randomising a baby. Randomisation website automatically ‘talks’ to OpenClinica to create this form for you.

Respiratory Support Log

Infant's date of birth

2020-01-19

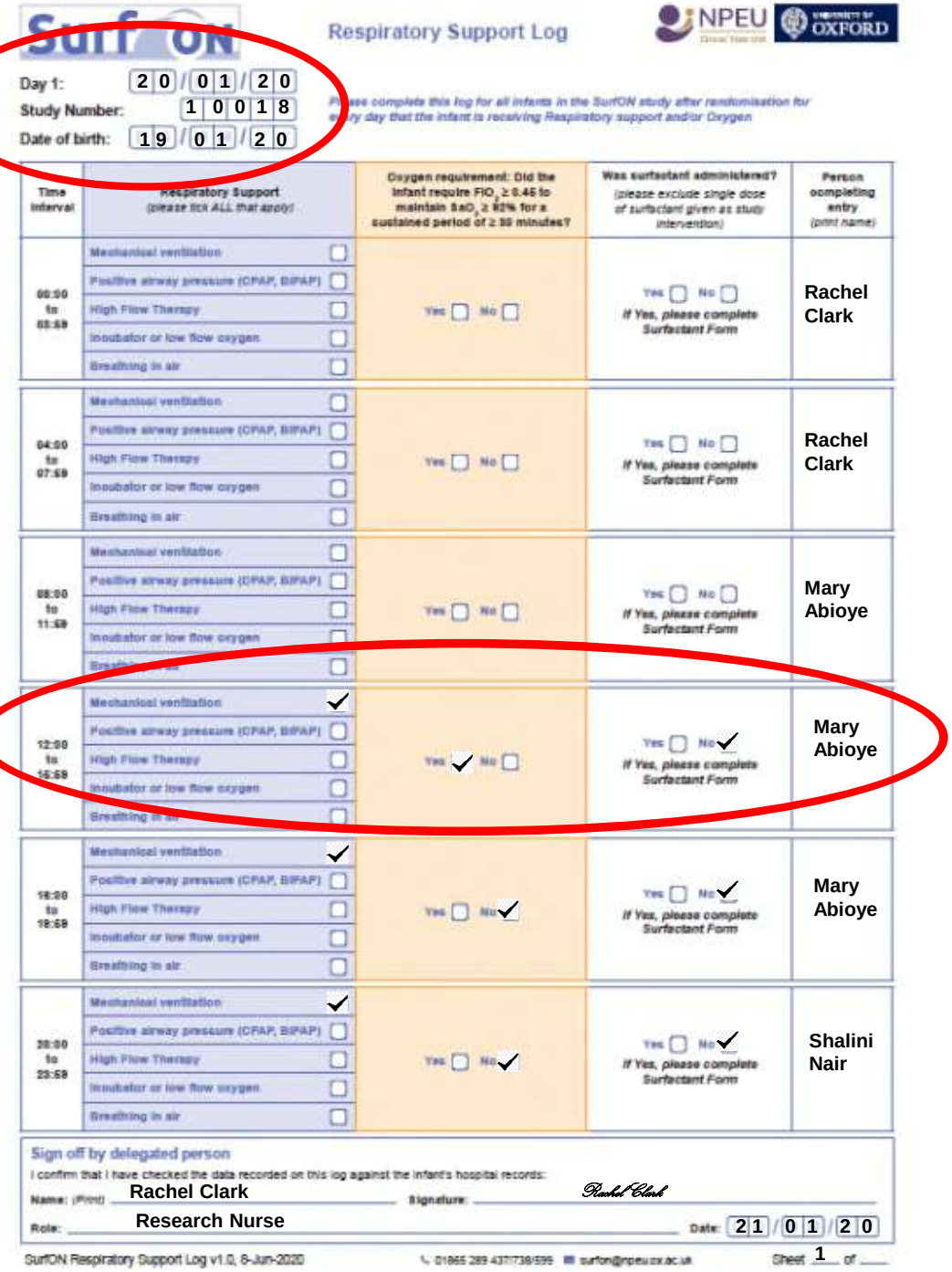
Date of randomisation	Time of randomisation
2020-01-20	14:45

Respiratory support log

Date	Time interval	Respiratory Support	Did the infant require $FiO_2 \geq 0.45$ to maintain $SaO_2 \geq 92\%$ for a sustained period of ≥ 30 minutes?	Was surfactant administered? Please exclude single dose of surfactant given as study intervention
2020-01-20	12:00 to 15:59	☑ Mechanical ventilation ☐ Positive airway pressure (CPAP, BiPAP) ☐ High flow therapy ☐ Incubator or low flow oxygen ☐ Breathing in air	◉ Yes ○ No	○ Yes ◉ No
2020-01-20	16:00 to 19:59	☐ Mechanical ventilation ☐ Positive airway pressure (CPAP, BiPAP) ☐ High flow therapy ☐ Incubator or low flow oxygen ☐ Breathing in air	○ Yes ○ No	○ Yes ○ No

+

Paper Log data entry would begin based on date and time of randomisation



SurfON — Surfactant Or Not

Respiratory Support Log

NPEU — University of Oxford

Day 1: 20/01/20

Study Number: 10018

Date of birth: 19/01/20

Please complete this log for all infants in the SurfON study after randomisation for every day that the infant is receiving Respiratory support and/or Oxygen

Time Interval	Respiratory Support (please tick ALL that apply)	Oxygen requirement: Did the infant require $FiO_2 \geq 0.45$ to maintain $SaO_2 \geq 92\%$ for a sustained period of ≥ 30 minutes?	Was surfactant administered? (please exclude single dose of surfactant given as study intervention)	Person completing entry (print name)
00:00 to 03:59	Mechanical ventilation ☐ Positive airway pressure (CPAP, BiPAP) ☐ High Flow Therapy ☐ Incubator or low flow oxygen ☐ Breathing in air ☐	Yes ☐ No ☐	Yes ☐ No ☐ *If Yes, please complete Surfactant Form*	Rachel Clark
04:00 to 07:59	Mechanical ventilation ☐ Positive airway pressure (CPAP, BiPAP) ☐ High Flow Therapy ☐ Incubator or low flow oxygen ☐ Breathing in air ☐	Yes ☐ No ☐	Yes ☐ No ☐ *If Yes, please complete Surfactant Form*	Rachel Clark
08:00 to 11:59	Mechanical ventilation ☐ Positive airway pressure (CPAP, BiPAP) ☐ High Flow Therapy ☐ Incubator or low flow oxygen ☐ Breathing in air ☐	Yes ☐ No ☐	Yes ☐ No ☐ *If Yes, please complete Surfactant Form*	Mary Abioye
12:00 to 15:59	Mechanical ventilation ✓ Positive airway pressure (CPAP, BiPAP) ☐ High Flow Therapy ☐ Incubator or low flow oxygen ☐ Breathing in air ☐	Yes ✓ No ☐	Yes ☐ No ✓ *If Yes, please complete Surfactant Form*	Mary Abioye
16:00 to 19:59	Mechanical ventilation ✓ Positive airway pressure (CPAP, BiPAP) ☐ High Flow Therapy ☐ Incubator or low flow oxygen ☐ Breathing in air ☐	Yes ☐ No ✓	Yes ☐ No ✓ *If Yes, please complete Surfactant Form*	Mary Abioye
20:00 to 23:59	Mechanical ventilation ✓ Positive airway pressure (CPAP, BiPAP) ☐ High Flow Therapy ☐ Incubator or low flow oxygen ☐ Breathing in air ☐	Yes ☐ No ✓	Yes ☐ No ✓ *If Yes, please complete Surfactant Form*	Shalini Nair

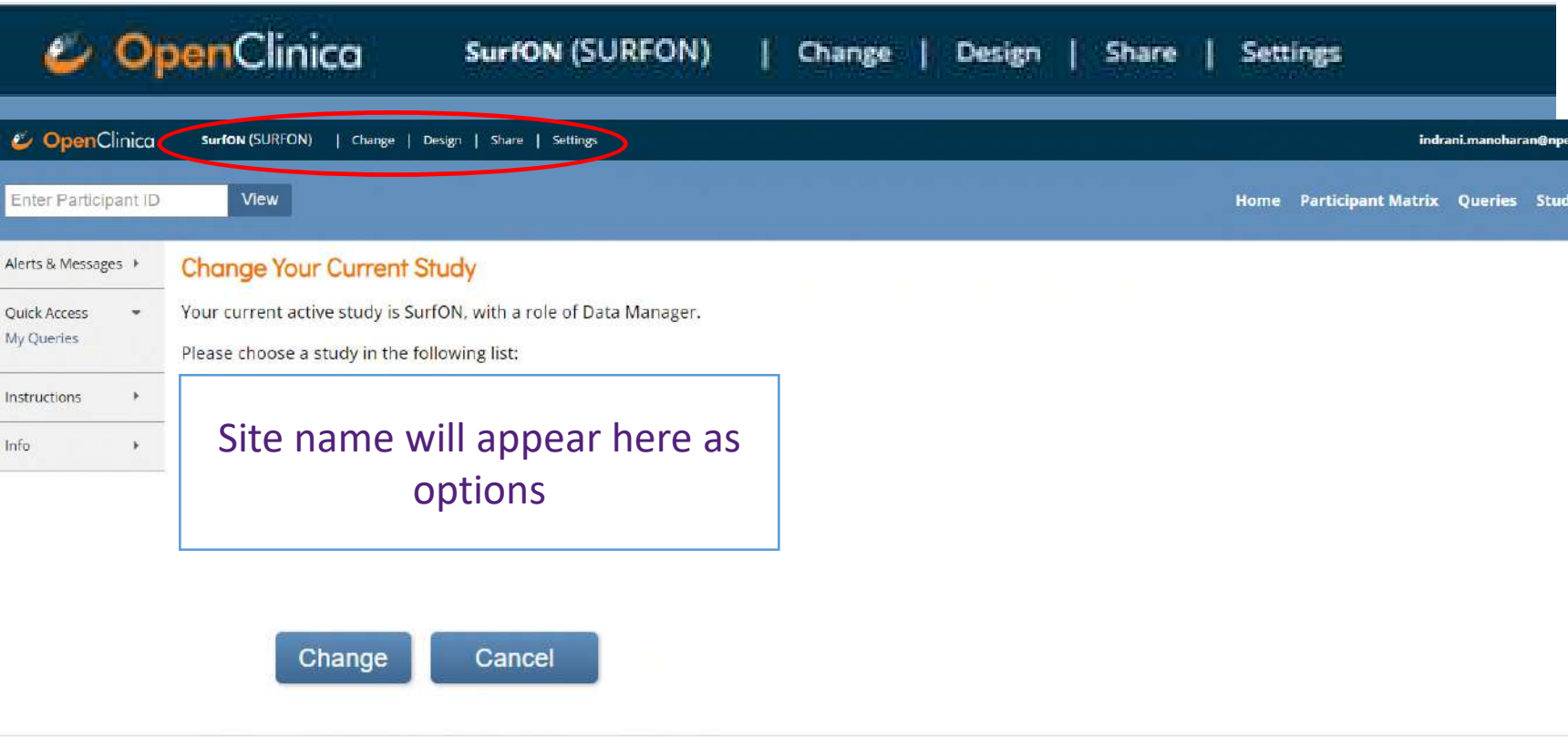
Sign off by delegated person

I confirm that I have checked the data recorded on this log against the infant's hospital records:

Name: (Print) Rachel Clark Signature: Rachel Clark

Role: Research Nurse Date: 21/01/20

OpenClinica access if the trust has multiple hospital sites that are recruiting



- Use the link provided to open OpenClinica for Site 1 (eg, Royal Derby Hospital), users can then see the option **"Change"** in the bar at the top of the screen (near the OpenClinica logo):
- Click on the **"Change"** link and you would then have the option to select Site 2 (eg, Burton hospital instead of Royal Derby Hospital). If you select site 2 and then click the Change button at the bottom of the page, you should be able to access data for recruits based at Site 2

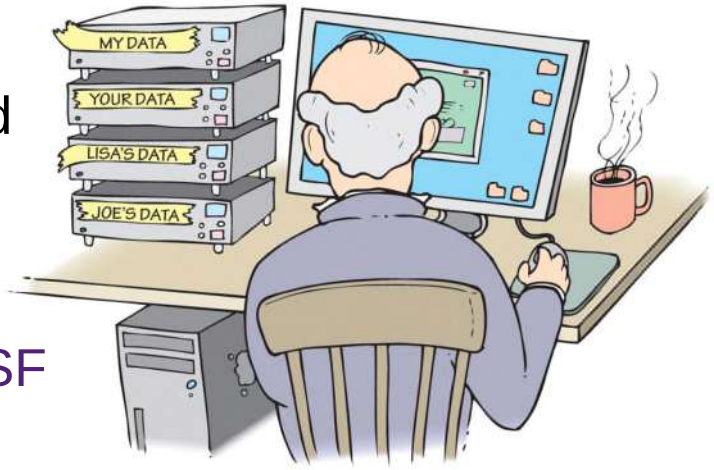
Part II - Presentation overview

- **DATA MANAGEMENT**
  - Case Report Forms
  - How data is collected throughout the trial period
  - Completing Screening logs
  - Study database –Openclinica

- **MONITORING & ARCHIVING**

Central Monitoring & Site Visits

- Remote central monitoring is conducted routinely at monthly Project Management Group meetings
- For eg, Surfactant administration, Consent Forms, Delegation log, Safety Reporting, CRFs etc are checked remotely
- Where Site monitoring is triggered, SurfON Study Team will liaise with the local staff member to arrange for a visit
- Site Monitoring Visit Report will be provided highlighting any issues / action plan
- A copy of the report should be filed in the ISF



Archiving

- Ensure that the Investigator Site File (ISF) and all study documents are archived appropriately when notified by the Sponsor or SurfON Study Team and retained as required by the Protocol

- Essential study documents need to be archived once all study-related activity is completed and Clinical Trial Summary Report is available

- Because our study involves minors under 18 years old, essential documents should be archived for a minimum of 25 years
- Documents need to be stored in a way that preserves their accuracy, integrity and legibility, and restricts access to authorised individuals only
- No additional funding provided for archiving

PART III – Study Documentation & Administration

Part III - Presentation overview

- **STUDY DOCUMENTATION**
  - ISF & Site Documents Box
  - Site Training Log & Delegation Log
  - CV & GCP
  - Data Collection File

- **WHAT'S NEXT?**
  - Recruitment following Sponsor Green Light (new sites only)

- **STUDY ADMINISTRATION**
  - Reordering of supplies
  - Out-of-hours helpline

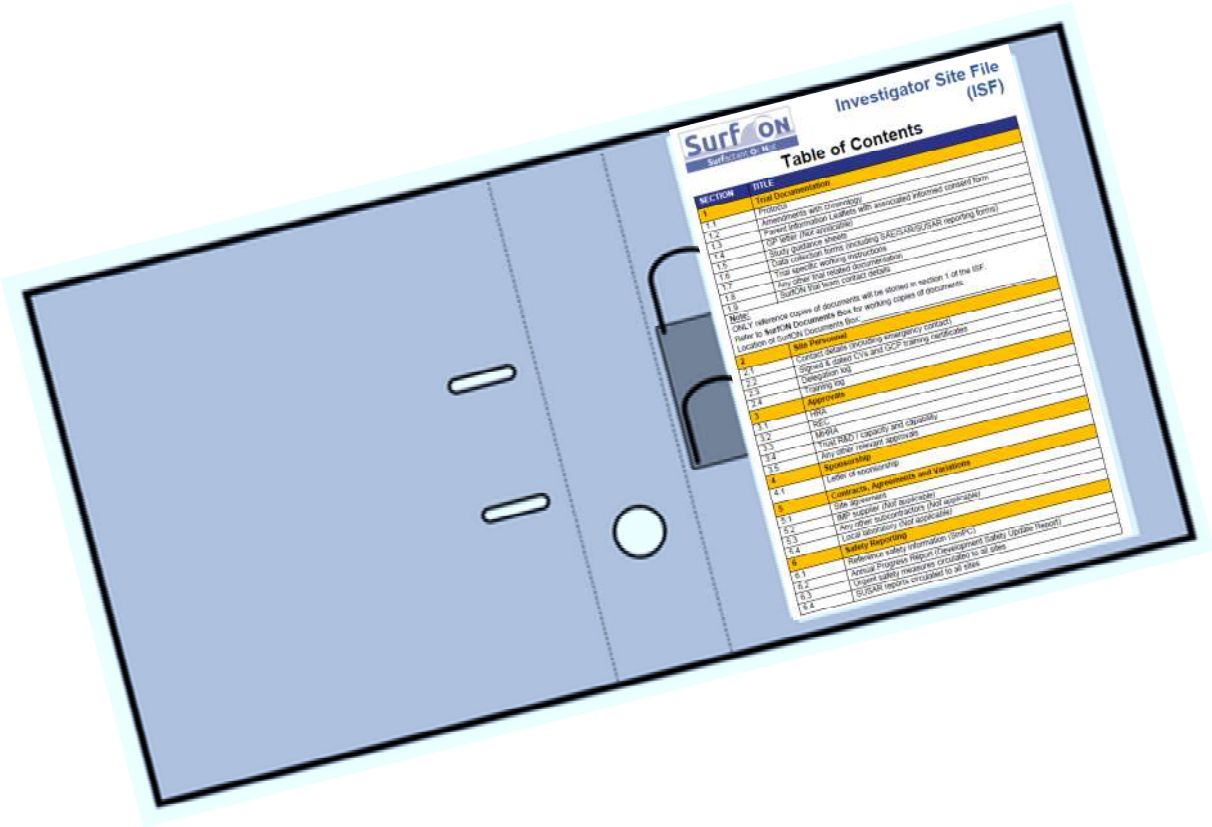
Study Documentation for Sites

SurfON Site Documents Box

Contents:
-Investigator Site File
-Data Collection File
-Extra copies of PIL, consent forms,
Respiratory support logs, guidance sheets etc.

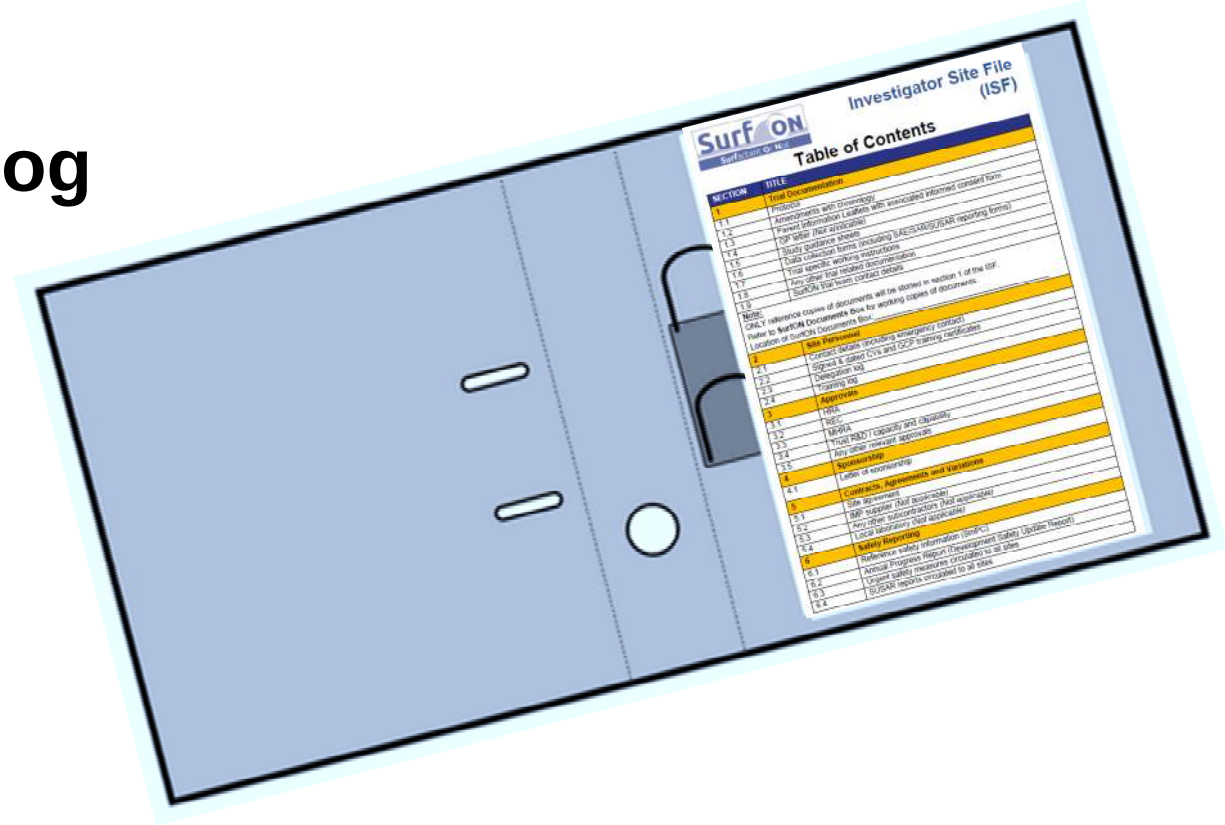
Investigator Site File (ISF)

- Study documentation – single copy
- Consent forms
- Training log
- Delegation log
- CV, GCP
- Approvals
- Sponsorship
- Agreements
- SmPC
- Site visits
- File notes
- Screening log
- Incident forms



Investigator Site File (ISF)

- Study documentation – single copy
- Consent forms
- **Training log**
- **Delegation log**
- CV, GCP
- Approvals
- Sponsorship
- Agreements
- SmPC
- Site visits
- File notes
- Screening log
- Incident forms



Training Log

Study Title.....: *Multicentre, open-label, randomised controlled trial of early surfactant therapy versus expectant management in late preterm and early term infants with respiratory distress.*

Chief Investigator.....: *Professor Elaine M Boyle*

Site Name:	**Investigator:**	**IRAS ID.....:** 269023 **REC Ref.....:** 20/EM/0003 **EudraCT no...:** 2019-003764-45
University Hospitals of Leicester NHS Trust	Prof Elaine M Boyle	

Trainee Name	Study Role	Trainee Signature	Training Description	Trainer Name/ Organisation	Date *(dd/mm/yy)*	Trainer Signature
Rose Garr	Research Nurse	Rose Garr	SIV	Indrani Manoharan	17/06/20	indrani m
Rose Garr	Research Nurse	Rose Garr	OpenClinica & Randomisation website	Dave Arch	22/06/20	Dave

- ✓ Please ensure your training logs are routinely maintained & kept updated (for example- to document OpenClinica training or SurfON SIV training delivered locally)
- ✓ However, training logs are kept mainly at site for site reference. Please scan and send training log to surfon@npeu.ox.ac.uk

Delegation Log

NPEU Clinical Trials Unit

SurfON Surfactant Or Not

PM107-B

Site Delegation Log

Study Name:	**SurfON** EudraCT No: 2019-003764-45	**Title:**	Multicentre, open-label, randomised controlled trial of early surfactant therapy versus expectant management in late preterm and early term infants with respiratory distress.	**Page _____ of _____**
Hospital:		**Principal Investigator:**		

Legend

Use this legend to complete the "Responsibilities" column on the next page. For each individual listed in the "Full Name" column, enter the letter(s) (e.g. A, C, E) from the legend below that correspond to their study-related responsibilities. If there are significant protocol related responsibilities that are not already included in the legend, add them in the empty spaces provided below.

Remove/insert additional responsibilities as required

A	Screen Potential Participants	F	Data collection form completion/ Resolution to data queries (OpenClinica)/Sign-off Respiratory Support Log	K	
B	Confirm Eligibility (medically trained doctors & Advanced Neonatal Nurse Practitioners [ANNPs] only)	G	SAE clinical review/causality assessment & sign off (medically trained doctors only)	L	
C	Obtain Informed Consent (medically trained doctors, ANNPs & nurses)	H	Maintain Investigator Site File	M	
D	Randomisation	I	All of the above responsibilities (usually PI, Co-PI or Associate PI)	N	
E	Provide Study-related Training	J	Other (specify):	O	
Note: Responsibilities A, D, E, F, H can be completed by any trained & delegated site staff					

The Principal Investigator should sign below during the **Site Close-Out Visit.**

I have reviewed the information on this log and have found it to be accurate. All delegated duties were performed with my authorisation.

Principal Investigator Signature: _____ **Site Close-Out Visit Date:** _____

Delegation Log

Study Name:	**SurfON** EudraCT No: 2019-003764-45	**Title:**	Multicentre, open-label, randomised controlled trial of early surfactant therapy versus expectant management in late preterm and early term infants with respiratory distress.
Hospital:		**Principal Investigator:**	

This log should include all relevant study staff and other clinical staff who routinely carry out study procedures or who have specific data collection/interpretation responsibilities.

Add new or replacement staff as appropriate. Please send updated copies to the surfon@npeu.ox.ac.uk

Note: Please complete the log and obtain the PI's approval before starting study-related responsibilities.

							Delegated Individual		Principal Investigator	
FULL NAME *(PLEASE PRINT)*	**ROLE**	**RESPONSIBILITIES** *(USE CODES LISTED ABOVE)*	**DATES OF RESPONSIBILITIES**		**EMAIL ADDRESS**	**APPRO-PRIATE GCP?** ✓	**USUAL INITIALS**	**SIGNATURE**	**PI'S SIGNATURE**	**DATE**
			FROM	**END**						

- ✓ **Please ensure your local Principal Investigator (PI) has delegated responsibility (signed off) for staff on the SurfON Site Delegation Log; This is quite often missed therefore leading to reportable incidents & breaches.**
- ✓ **Associate PIs (NIHR scheme) cannot sign off other staff members in line with guidance. Co-PIs are able to sign off other staff members if delegated for that responsibility by PI.**
- ✓ **Multiple hospital sites (under a single NHS trust) can maintain separate delegation logs.**
- ✓ **Whenever the log is added to or updated, please remember to scan in the 'entire log' and send the updated log to surfon@npeu.ox.ac.uk.**
- ✓ **Only GCP and CV for the PI, APIs, Co-PIs and lead nurse(s) are submitted to the SurfON Study team; Please maintain records locally for all other staff members and need not be submitted.**

Site Delegation Log – Some Top Tips !

1. Please take care to complete and maintain your Site Delegation Log, to avoid incidents and serious breaches !

2. **Site staff** who have **completed all the essential training** related to SurfON should enter their details onto the log

3. Ensure that all the **columns in the log are correct and complete**, especially the responsibility codes

4. Insert the date for the 'start date' of your duties. However, only when the PI signs, the date of the **PI's signature indicates the start of your duties**.

5. **Do not strike through** an entry on the log

6. If there is an **error** or you need to update an entry, then complete a new line for that individual in the log

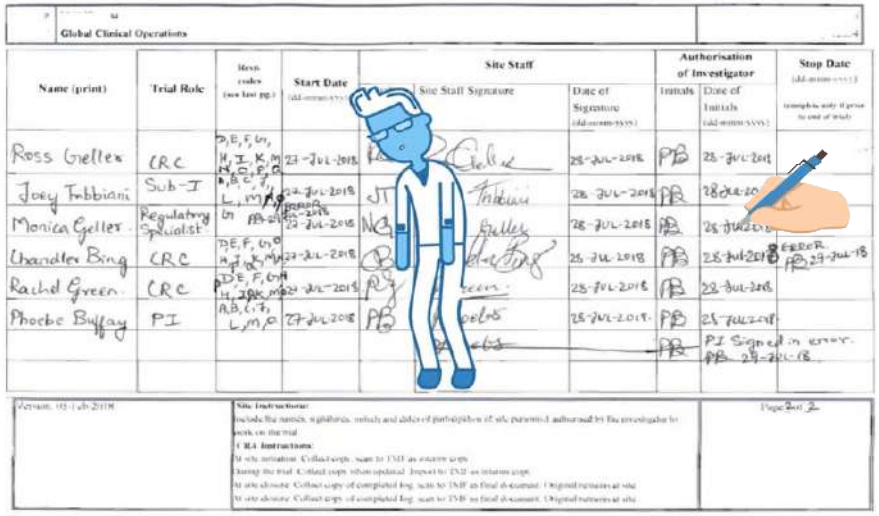
7. If an individual is on the log, but then assumes **a new responsibility** e.g consent, don't add a new responsibility code to their entry. **You must complete a new line**. In this instance, add an 'end date' to their previous entry and make sure the 'start date' of their new entry corresponds to the end date entered

8. Always maintain '**end dates' for any staff who leave** – this is especially important if clinical staff rotate during the year

9. **CV & GCP:**
PI is responsible for collecting evidence of **appropriate training** for all other staff delegated to take part in the study activities

SurfON – common trial deviations !

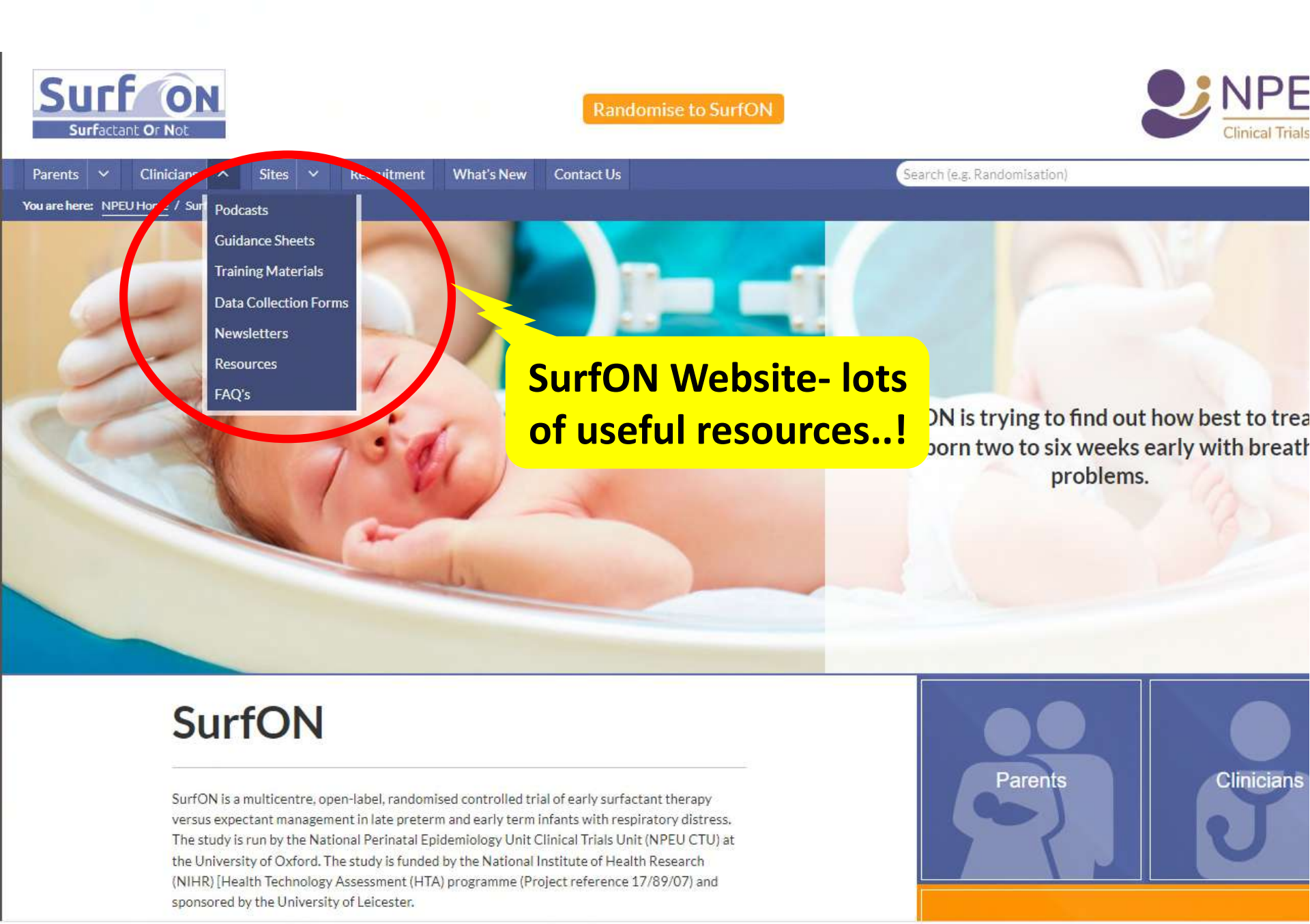
Delegation Log



- Delegation log erorrs
- Consent form errors
- Submitting personal identifiable information (eg, consent form) to surfon@npeu.ox.ac.uk instead uploading it on the **NPEU CTU Document Upload Tool**
- Missed data collection (eg, respiratory support logs)

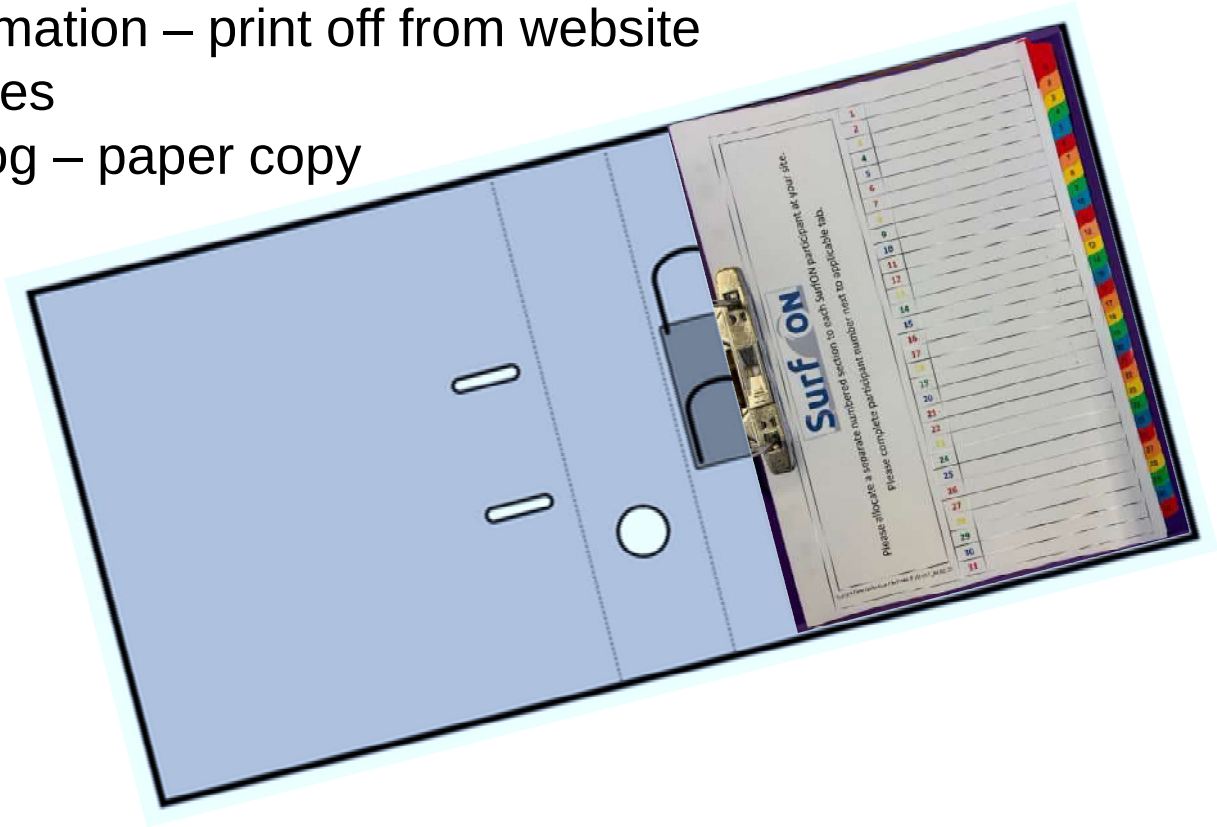
Incidents & deviations create administrative burden for both the sites and SurfON study team

Please get in touch with SurfON team for queries & routinely utilise SurfON website for guidance sheets & resources


SurfON
Surfactant Or Not
Randomise to SurfON
NPE
Clinical Trials
Parents
Clinicians
Sites
What's New
Contact Us
Search (e.g. Randomisation)
You are here:
Podcasts
Guidance Sheets
Training Materials
Data Collection Forms
Newsletters
Resources
FAQ's
SurfON Website- lots of useful resources..!
problems.
SurfON
SurfON is a multicentre, open-label, randomised controlled trial of early surfactant therapy versus expectant management in late preterm and early term infants with respiratory distress. The study is run by the National Perinatal Epidemiology Unit Clinical Trials Unit (NPEU CTU) at the University of Oxford. The study is funded by the National Institute of Health Research (NIHR) [Health Technology Assessment (HTA) programme (Project reference 17/89/07) and sponsored by the University of Leicester.
Parents
Clinicians

Data Collection File

- Randomisation confirmation – print off from website
- Mother's questionnaires
- Respiratory support log – paper copy
- SAE forms
- Incident forms



Note:

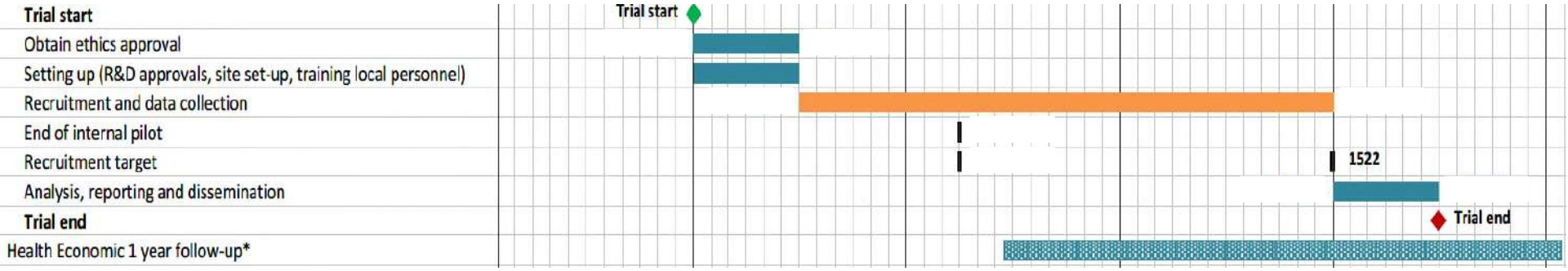
X No Pharmacy Site File

X No Accountability Logs

X No IMP labelling

https://www.brickunderground.com/live/introducing-new-baby-to-building

SurfON trial plan & COVID-19 impact



- Recruitment was due to commence after March 2020
- COVID-19 impact & adverse impact on all research
- NIHR – review of all studies after COVID-19; SurfON being one of them
- SurfON went on pause from Feb 2022 to May 2022
- Recruitment recommenced 04 Jul 2022
- Inviting further NHS sites to register interest to participate (>45 sites)
- Key trial updates & dates will be advised

SurfON recruitment phase

Target: 1,522 babies
at least 1-2 babies per month per site!

We are looking for SurfON Champions to help us recruit at least

1-2 Babies Per Month at every site

Could YOU be our local Champion?

NIHR | National Institute for Health Research

SurfON has been enrolled on the

NIHR CRN Associate Principal Investigator Scheme

Associate PI Scheme – Structure

- Open to any doctor, nurses and AHPs willing to make a significant contribution to the conduct and delivery at a local level. The scheme is not open to those who are funded to work on research, such as Research Nurses.

- Participation in the Associate PI Scheme does not absolve local PIs of their responsibilities at site. Local PIs will act as mentors to their Associate PI.

- Commitment of at least 6 months will be required for gaining Associate PI status.

- Must register prospectively- retrospective recognition is not possible

Benefits of the Associate PI Scheme

For the Associate PI

- Experience of research - able to contribute to the conduct and delivery of a study at local level with the oversight of the local enthusiastic PI.
- Learns about the challenges and practicalities of delivering a portfolio study, understands the responsibilities associated with the PI role, and their participation is recognised through certification for their CPD portfolio.
- Associate PIs will be acknowledged in the primary publication(s) from the study, which will be defined upfront on an individual trial basis.

For the PIs

- Additional support with the delivery of the study
- Play a part in developing the PIs of the future

For CTUs

- Increased support for the trial at sites- managing delegation logs etc
- Speedier delivery

For the Patients

- Increased opportunities to be involved in high- quality research

Associate PI Scheme - How to Register

Go to the NIHR Associate PI Scheme Website :
https://www.nihr.ac.uk/documents/associate-principal-investigator-pi-scheme/25040

To register yourself as an Associate PI, complete the Associate PI Scheme Applicant Registration Form


NIHR | National Institute for Health Research

Associate PI Scheme - Applicant Registration Form

This form should be completed by applicants wishing to register for the Associate PI scheme.

If you would like to apply for Covid-19 Urgent Public Health studies, please use the form at the following link:
https://docs.google.com/forms/d/e/1FAIpQLSc-y-Y_qql42hFkznZk_eZLCNkCq7liUYZkiI4I0Kxy0nDykQ/viewform

The scheme has been endorsed by the NIHR Clinical Research Network and the following Royal Colleges:

SurfON recruitment phase

What we request from you?

- Delegation & training logs
- CV & GCP for relevant staff
- OpenClinica & Randomisation website training & SIV (study training) to be completed
- Team photo requested
- mNCA (Per Participant Payment) agreement signature (tripartite)
- Local R&D Capacity & Capability confirmation to recruit at least **1-2 Babies Per Month** per site
- SurfON team will provide regular updates on key trial progress
- Ensure team are trained and enough members are delegated to conduct trial activities, improve local trial awareness/training using materials on website
- Sponsor Green Light (SGL) will be issued for new sites before recruitment can commence. Recruitment can begin **only** after SGL

Surf ON
Surfactant Or Not

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Chief Investigator
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Pauline Rushby
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Zainab Aslam
Data Co-ordinator/Administrative Assistant
01865 289428

NPEU CTU, University of Oxford

- Pollyanna Hardy (Director, NPEU CTU)
- Charles Roehr (Clinical Director, NPEU CTU)
- Christina Cole (Senior Trial Manager)
- Ann Kennedy (Assistant Trials Manager)
- Andy King (Head of Trials Programming)
- David Murray (Senior Trials Programmer)
- Kayleigh Stanbury (Head Of Operations)
- Joy Wiles (Quality Assurance Manager)
- Richard Welsh (Senior Software Developer)
- Madeleine Hurd (Data Manager)

Co-Investigators

- Marie Hubbard (Neonatal Research Nurse)
- Ed Juszczak (Medical Statistician)
- Oliver Rivero-Arias (Health Economist)
- Ben Stenson (Neonatologist)
- David Sweet (Neonatologist)
- Bliss Charity

Out-of-Hours Helpline:

In the case of **urgent out-of-hours** queries, please phone **0800 138 5451**.

When you call this number (freephone), you will be put through to a call centre which provides 24-hour emergency support. They will ask for the following before they can address your query:

1. your name
2. the hospital you are calling from
3. your full phone number
4. the name of the trial (SurfON)

Thank you for listening

Questions?

SurfON Study Team

NPEU Clinical Trials Unit
University of Oxford
Old Road Campus
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Oxford OX3 7LF

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W: www.npeu.ox.ac.uk/surfon

@SurfONtrial https://twitter.com/SurfONtrial
#surfontrial

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The views expressed are those of the author(s) and not necessarily those of the NIHR or the Department of Health and Social Care.