SurfON Frequently Asked Questions (FAQs)

Clinical FAQs:

1. **What is the current practice with regard to management of respiratory distress for late preterm and early term infants?**

   There is no research evidence to guide the management of respiratory distress in this group of infants and no clinical consensus. As a result, practice varies substantially, according to individual clinicians' opinions, preferences and prior experience. Many clinicians use non-invasive respiratory support (nasal CPAP or nasal high flow therapy) as the first line of intervention, though this is not universal. Some clinicians prefer to administer surfactant early in the course of the illness to prevent deterioration, while others adopt a "watch and wait" approach, and only intervene if the infant's condition mandates this. It is likely that a variety of approaches fall between these two ends of a spectrum. Thresholds for intervention are also widely variable, with some clinicians being comfortable to accept significant oxygen requirements in infants on non-invasive respiratory support without intervening.

2. **Why are there no RCTs conducted in this group so far to provide an evidence based approach?**

   In the past, late preterm and early term infants were among the most immature to survive. They experienced significant respiratory problems and many died of their respiratory disease. Advances in modern obstetric and neonatal care such as antenatal corticosteroids and advanced neonatal respiratory support have made this an unusual occurrence. This has led to these infants being regarded and managed in a similar way to full term infants (born at 39–41 weeks). It is only in recent years that researchers have begun to question the appropriateness of this, based on data from observational studies. These studies have highlighted increased mortality and worse short and long term outcomes in late preterm and early term infants, when compared with their full term counterparts. These reports are consistent in their conclusions, and it is now recognised that interventional studies are now required to determine optimal practice for many aspects of clinical practice in this population. To our knowledge, SurfON is the first multicentre RCT to focus on late preterm and early term infants.

3. **Will this study pave the way to a change in practice for these infants?**

   Optimal management of very preterm infants with respiratory disease has been guided, refined and standardised over years through a series of well-designed research studies and trials. There is now a need to define best practice for more mature infants with respiratory distress, in whom there is a lack of robust research. We very much hope that the successful completion of SurfON will go some way towards optimising the management of these infants, and that practice will then become evidence-based, rather than "opinion-based".

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4. **What is considered as lack of trial equipoise? How can we address this at our site?**

   To be in clinical equipoise for any trial requires acknowledgement of the fact that, as a group of neonatal clinicians, we do not know how best to manage a problem in a given population in order to optimise outcomes. This is a key factor in any RCT that compares two different approaches to the same problem.

   We know that between sites and between clinicians, differences of opinion exist based on individuals' prior experience and long-held views. This is understandable when there is a lack of evidence, and these differences may be extreme in some cases. Nevertheless, it is clear that if an "optimal" approach exists to improve short and long term outcomes for the majority of this large group of infants, it will never be found if clinicians maintain fixed views, adopt their "own" approach and are unable to recognise that there may be other, and perhaps even better strategies. Where variation in practice exists and is very marked, the only way to determine best practice is through well-designed research and RCTs to test reasonable hypotheses.

   If there are widely differing views within your unit about managing late preterm and early term infants, it may help to study the published evidence – there is little if any robust data, but a recent systematic review (Ramaswamy et al. Surfactant therapy in late preterm and term neonates with respiratory distress syndrome: a systematic review and meta-analysis. Arch Dis Child Fetal Neonat Ed 2021) - https://fn.bmj.com/content/fetalneonatal/early/2021/10/21/archdischild-2021-322890.full.pdf may be helpful. It can also be useful to meet as a group and discuss any differences of opinion and how these can be overcome. The Chief Investigator for SurfON will also be very happy to discuss the rationale behind the study with your team, and this can be arranged either online or in person, as preferred.

5. **Could you clarify rationale behind excluding infants with major structural or chromosomal abnormality? What are the reasons behind the exclusion criteria?**

   As SurfON is a study of Early Surfactant Therapy compared with Expectant Management, we hope to avoid recruiting any infants who have other obvious reasons for their respiratory distress that would neither be amenable to treatment with surfactant nor spontaneously recover. This would include infants with congenital respiratory or cardiac abnormalities, chromosomal abnormalities that are commonly associated with multiple additional problems and/or limited survival, or known neurological or neuromuscular conditions that would affect respiratory muscles or respiratory drive or other conditions requiring early surgery. Should any of these diagnoses be suspected or confirmed after enrolment to the study, please do not withdraw the infant, but do make us aware of this.

6. **When and how should we approach parents to discuss the SurfON Study?**

   Where a mother is expected to deliver at 34–36 weeks of gestation, we feel it is acceptable to discuss the study before delivery, stressing that the infant would only be eligible if he/she had breathing problems. It is not appropriate to speak to parents at 37–38 weeks of gestation, as this would cause undue anxiety when most of these infants would never be eligible.

Whenever parents are approached, they should be made aware that different doctors prefer different approaches to manage breathing problems in infants like theirs, but that we do not know which is best. Some infants get better on their own and others get worse but it is not easy to predict. The study is trying to find out whether it is better to give medication into the lungs early, or wait to see if the infant gets better without medication. Both of these two different approaches are routinely used across the country, depending on the doctors' preferences.

For infants born at 34–38 weeks of gestation who need admission to a neonatal unit with respiratory distress, we recommend speaking to the parents as early as possible after the decision for admission has been made. Infant's conditions can change rapidly at this early stage and it is often helpful to have discussed the study with parents even before the infant meets eligibility criteria. Parents then have time to watch the study video, read study information and consider whether they would wish to participate in the study if their infant becomes eligible. They should be made aware that if the infant becomes eligible, then we would like to enrol the infant as soon as possible. If they are willing to offer consent at this time, this is acceptable. If the infant then recovers quickly, it is a simple matter to let them know that, happily, their infant is no longer eligible. Should an infant become ineligible due to an acute and profound deterioration where there is no longer a position of equipoise, then that infant should not be randomised.

7. **Why is a radiological diagnosis of Respiratory Distress Syndrome (RDS) through routine Chest X-Ray (CXR) not included as inclusion criteria?**

   SurfON is looking at the management of infants with clinical signs of respiratory distress. There is no requirement to confirm a diagnosis of RDS with a chest x-ray or any other investigation and many infants may meet clinical eligibility criteria before an x-ray would usually be performed. In addition, the appearances of chest x-rays are often non-specific. We acknowledge that an infant may have a respiratory diagnosis other than RDS, such as transient tachypnoea of the newborn (TTN), chest infection, meconium aspiration etc. However, many other respiratory diagnoses are characterised by secondary surfactant deficiency making it reasonable to recruit to SurfON. In addition, surfactant therapy has been studied in many different respiratory conditions and has been shown either to be potentially beneficial, or not harmful.

8. **What if the infant has had a chest x-ray and this shows a pneumothorax? Is the infant eligible?**

   Pneumothoraces and other air leaks vary in size and severity. It is expected that, in the case of any identified air leak, the attending clinician will use clinical judgement to decide whether it is appropriate and safe to recruit the infant to SurfON. Data about air leaks is being collected as a secondary outcome for the study.

9. **Is there a requirement for a cranial ultrasound scan to be performed?**

   In many neonatal units, it is not usual to routinely carry out cranial ultrasound scans in more mature infants, as the risk of serious intracranial haemorrhage is low in comparison with that in very preterm infants. We do not require a cranial ultrasound as part of the study, but will collect data on neurological complications as a secondary outcome.

10. **Why is 0.45 FiO2 chosen as the threshold for severe respiratory failure?**

    SurfON is a pragmatic clinical study. To achieve adequate separation between the two randomised groups, it is extremely important that infants randomised to Expectant Management are given a reasonable period of time on non-invasive respiratory support alone before any further intervention. The co-primary outcome of "severe respiratory failure" is defined as ≥30 minutes in ≥45% oxygen to maintain oxygen saturation of ≥92%. This was determined by consensus among the clinical co-investigators and after discussion with other colleagues and was felt to be the point at which some clinicians would start to consider intervention.

11. **If an infant in either arm meets the criteria for "severe respiratory failure", do we have to give surfactant and/or intubate the infant?**

    For our definition of severe respiratory failure, we believe that we have chosen the point at which many clinicians would start to feel uncomfortable about continuing without intervention. However, we also know that this is not the case for all, and there is NO REQUIREMENT TO INTERVENE at this point if this would not be your usual practice. Please take whatever action you feel is appropriate – if your usual practice would be to continue a "watch and wait" approach, please do so.

12. **If we are unhappy about an infant's condition, can we intervene even if the criteria for severe respiratory failure have not been reached?**

    We hope that clinicians will continue Expectant Management on non-invasive respiratory support for as long as they feel able do so, in the hope that the infant will recover without further intervention. However, if a senior clinician feels it is no longer safe to continue without intubation and/or surfactant, then please take whatever action is felt to be required for the infant's safe ongoing care.

13. **Can surfactant be administered after the 24 hour 'cut-off'?**

    The SurfON study hypothesis is that proactive management with EARLY surfactant will be beneficial in reducing severity of respiratory illness and length of stay. We believe that most mature infants with respiratory distress will meet eligibility criteria well before the 24 hour recruitment period ends. We urge units to approach parents as early as possible in the course of their infant's illness, in order to be able to successfully test this hypothesis. Infants that are going to recover spontaneously and quickly usually do so within the first few hours after birth. Any infant who is thought to still require respiratory support, either with or without oxygen after one or two hours is likely to be eligible for recruitment. We therefore anticipate that most infants who have had respiratory distress from

birth, or soon after birth will be recruited to the study very much earlier than 24 hours. For any infant randomised to the early surfactant arm, please give the surfactant as soon as possible after randomisation.

14. **What happens if surfactant is administered to a participant in the Expectant Management group before the thresholds have been met?**

    The study intervention for those randomised to Early Surfactant Therapy is a single dose. If surfactant is given to any infant in either group that is additional to the requirement for their randomised group please complete a Surfactant Form. This does not constitute as a withdrawal or an incident for reporting, however the reasons behind administration should be clearly documented. If there are any concerns around this, please contact the SurfON study team.

15. **What dose of surfactant should be given to multiples?**

    Twins and higher order multiple births where more than one infant is eligible for the study will be randomised to the same study arm. As usual in routine practice, the appropriate dose of surfactant should be given for the individual infant's weight and according to manufacturer's guidance (100-200 mg/kg), according to usual unit practice.

Generic FAQs:

General Questions

1. **Is SurfON a national study?**

   Yes, SurfON is taking place in all UK nations – England, Scotland, Wales and Northern Ireland.

2. **Can Special Care Units participate in the study?**

   Yes, the study is open to Neonatal Intensive Care Units (NICUs), Local Neonatal Units (LNUs) and Special Care Units (SCUs).

3. **Who can be a Principal Investigator (PI)?**

   Applications to be a PI will be assessed on a case by case basis. We are happy to receive applications from both doctors and nurses.

4. **What is the recruitment target?**

   We are aiming to include 1,522 infants across ~45 sites with a minimum recruitment target of at least 1-2 infants per month per site.

5. **Can participants be enrolled into SurfON and another study?**

   Enrolment in another research study is does not exclude infants from participation in SurfON, and we are not aware of any conflicting studies. However please get in touch with SurfON study team if you have any further queries or concerns around this.

6. **Could you tell me more about the NIHR Associate PI scheme?**

   We are pleased to confirm that the SurfON (CPMS ID: 44406) has now been registered for the Associate PI scheme and has been listed on the List of Registered Studies on the NIHR Associate PI Scheme Website. The scheme is open to any doctor, nurse or AHP willing to make a significant contribution to the conduct and delivery of the study at a local level. The scheme is not open to those who are funded to work on research, such as Research Nurses. Local PIs will act as mentors to their Associate PI. The Local PI will continue to be the principle lead with overall responsibility for the trial at the site. Commitment of at least 6 months will be required for gaining Associate PI status. For further info please visit - https://www.nihr.ac.uk/health-and-care-professionals/career-development/associate-principal-investigator-scheme.htm

7. **What is the difference between Co-PI and Associate PI?**

   Staff members can register their interest to act as a Co-PI (essentially the same capacity as Associate PI) to the SurfON study team. However for this role there are no time limitations or assessments that the NIHR API scheme encompasses.

8. **Can we have both Co-PI and Associate PI at the site?**

   Yes, please get in touch with SurfON study team for further queries

9. **What is the SurfON Champion scheme?**

   If you are passionate about getting more people involved in research so that we can develop better care and treatment for these infants, then this is a perfect opportunity to volunteer as a SurfON Champion locally at your unit! You can help other healthcare professionals to understand why this study is important and help parents make informed decisions about study participation. With your permission, we would like to acknowledge you and your work as a Champion on our website. Your experience will also make a great addition to your CV. Please get in touch with the SurfON study team if you are interested.

Screening and Eligibility

10. **How can I improve awareness of the study in the unit? What tools can I use for this?**

    SurfON banners and posters that are approved by the regulatory authorities can be displayed in public areas to raise awareness of the study. We also have specific tools in the form of posters and stickers for use within clinical areas that could help with raising study awareness and also act as visible reminders for screening and recruitment.

11. Which infants will be screened and where?

All infants in the Neonatal Unit (NNU) born between 34+0–38+6 of gestation with respiratory distress can be screened for eligibility. Women in the Maternity Unit who are expected to deliver infants between 34 and 36 weeks of gestation can be screened for eligibility prior to delivery. Please refer to Guidance Sheet 1 for detailed information regarding screening.

12. How do I maintain screening logs?

At least once a month, please complete the screening details for your site on the Randomisation Website by visiting https://rct.npeu.ox.ac.uk/surfon/login.php. Paper screening logs are not expected to be returned to SurfON study team and are intended for internal use only.

13. Can we approach parents before the eligibility criteria has been met fully?

Yes, we recommend that early approach is key when 'potentially eligible infants' have been identified. We think this is key to avoid missing opportunities to include eligible infants on SurfON where informed consent has been provided. A parent friendly podcast available on SurfON website can be shared with the parents in order to introduce the study in lay language - https://www.npeu.ox.ac.uk/surfon or direct link https://youtu.be/y52cipynYiY

14. Who can confirm eligibility?

Final eligibility has to be reconfirmed at the point of randomisation by either a delegated clinician or Advanced Neonatal Nurse Practitioner (ANNP). Nurses *cannot* provide this even though they can obtain consent.

Informed consent

15. Is the Parent Information Leaflet (PIL) available in other languages?

No, all study documentation is only available in English. NHS translation services can be utilised as per standard care and if the clinical team deem that the parent has sufficient understanding about the study in order to provide full informed consent

16. Can under 16 year old mothers be included in 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 Fraser competent. For further information on this and legal parental responsibility, refer to Guidance Sheet 2 on informed consent.

17. Who can obtain consent from parents?

Clinicians, ANNPs and nurses can obtain consent for SurfON, as long as, prior to taking consent they have

- received SurfON training (eg. attended Site Initiation Visit (SIV) or trained by staff member delegated to provide study related training or completed training online by using training podcasts)
- been delegated the responsibility on SurfON Delegation Log and signed-off by the Principal Investigator (PI)
- completed GCP training
- been shown to comply with local policies and procedures that apply around obtaining consent on Clinical Trial Investigation for Medicinal Products (CTIMPs)

18. When should I do GCP refresher training?

This is normally required every three years, but Trust policies can vary. Sites only need to submit signed & dated CV and GCP for PI, lead research nurses (RN), Co-PI or Associate PIs. For all other staff members, the responsibility to maintain CV and GCP records is delegated to the local PI. Please note that GCP training can be completed as per trust policy and arrangements. For example, this could be via the NIHR website or could be local GCP training that the unit provides.

19. Who can give consent?

Ideally the birth mother should give consent but if consent cannot be obtained initially for any reason at the time, it may be obtained from the other parent (this could be same sex or opposite sex).

However *please obtain countersignature* from the mother as soon as possible following consent as the infant's participation on SurfON will not be valid unless mother provides countersignature.

20. What if the mother doesn't consent to completing the questionnaires?

It is acceptable for the mother to not provide consent for the optional part of the study i.e., to complete the study questionnaires related to quality of life and breast feeding. This does not exclude the infant from taking part in the main study.

21. How does the mother complete questionnaires if multiples are delivered?

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 SurfON Trial Entry Questionnaires.

22. What if the mother doesn't consent to be contacted for future studies?

Again, this is an additional part (point 9 of the consent form) and if the mother doesn't consent to this, it does not exclude the mother & infant from taking part in the main study and optional section to complete study questionnaires. This can be left blank.

23. Do both the parent giving consent and the health professional obtaining consent need to be on the same date?

Yes, this must be completed on the same day. Please be aware of this if consent occurs around 00:00.

24. Do I need to submit consent forms to the SurfON study team?

Yes, all consent forms must be scanned & emailed **ONLY** to ouh-tr.surfon@nhs.net from your nhs.net or trust email to ensure end-to-end encryption! This is because personal identifiable information is recorded in the consent forms.

Please note that copies of the consent forms must not be sent to the generic SurfON inbox (surfon@npeu.ox.ac.uk) as they would be considered as a study deviation.

Randomisation

25. When do we randomise an infant?

Infants should be randomised ≤24 hours of birth. Randomisation can be completed as soon as possible after consent and final eligibility confirmation (completed only by clinicians and ANNPs).

26. How do I randomise an infant?

Randomisation can be completed 24/7 online at https://rct.npeu.ox.ac.uk/surfon/login.php using the centre log-in details. Centre log-in details for the randomisation can be found on a sticker on the inside of the Site Documents Box (sent at the time of SIV). Alternatively, the log-in details are also provided in the Investigator Site File (ISF). If you have any issues, please contact surfon@npeu.ox.ac.uk

27. What do we do if we have issues randomising an infant?

If you experience technical difficulties with internet access or the Randomisation website use the emergency contact details provided in Guidance Sheet 9

28. Why do we need to complete the contact details form on the randomisation website?

It is important to record infant & mother's healthcare number, email address, postal address and phone number in order to complete remote follow up at one year's time (no direct contact involved) and also to communicate results from the study via email for those who wish to receive it.

29. How do multiples get randomised?

Randomisation occur on 1:1 ratio but multiples are randomised to the same study arm as this has been shown to be preferred by parents of twins and higher order multiples.

30. Do we need to maintain a respiratory support log for all infants regardless of which arm they are randomised to?

Yes, this is important, and it provides the data to be used for the **primary outcome** for the study!

For further information please refer to Guidance Sheet 5 on Case Report Forms (CRFs) and also watch training podcast at https://www.npeu.ox.ac.uk/surfon/clinicians/training-materials or using direct link https://youtu.be/tX2McF1gsMA

Study Intervention

31. What is the study guidance regarding surfactant administration?

CUROSURF® will be administered as per local site policy in line with the approved Summary of Product Characteristics (SmPC). The SmPC currently approved for use is dated 28 Jun 2018 available from https://www.medicines.org.uk/emc/medicine/21421#gref. Please note that the SmPC is reviewed annually and only study approved SmPC can be used.

32. What dose of surfactant will be given?

The recommended starting dose for the IMP is 100–200 mg/kg (1.25–2.5 ml/kg), administered in a single dose as soon as possible after randomisation. However, clinical judgement should be used and the correct dosage should be given as deemed clinically correct. If a second dose of surfactant is required, the same dosage should be administered.

33. Who can administer surfactant?

The administration of the IMP is dependent on local policy and procedure as there are no study specific requirements, e.g., this can be completed by ANNP or clinician.

34. What will be the mode of administering the surfactant?

Mode of administration will be as per local practice to include any of the following modes, for e.g., LISA, Insure and routine mechanical method. The mode of administration will be recorded on the electronic Case Report Forms (eCRFs) as will details of any sedation and medication given.

35. Which form(s) do I use to document administration of the surfactant?

The Surfactant Form is used to record additional doses of surfactant and for the administration of 'rescue' surfactant given to infants in the Expectant Management Arm.

The Intervention Form is only for the administration of surfactant to infants allocated to the Early Surfactant Therapy arm of the study.

36. How will infants be managed following the administration of surfactant?

Once infants have been administered CUROSORF®, they should be managed as per standard care.

37. Will SurfON supply the IMP?

No, CUROSURF® will be dispensed from hospital stock through routine prescription. There will be no over-labelling of the IMP, nor any pharmacy or accountability files. IMP supply will be managed as part of routine care.

Hospital Discharge

38. When should the SurfON Discharge Questionnaire be completed?

The mother should complete the questionnaire whilst in hospital just before the infant is discharge home. Please do not provide the questionnaire to be taken away for completion later on.

39. What do we do if we forget to administer SurfON Discharge Questionnaire?

In case it is missed for any reason, you have up to 7 days after infant's discharge to collect the data over the phone or via email by contacting the mother. Please note that visible reminders such as SurfON Discharge Questionnaire stickers are available for use in the clinical area either by the infant's cot side or on medical notes. If e-notes are being utilised please insert prompts in the system for completing data collection.

Follow up

40. Is there a follow up on the study?

Yes, follow up is completed remotely at one year of age corrected for prematurity using data linkage. Please enter correct NHS or health number along with other details in the contact details form on the randomisation website at the time of randomisation.

Safety Reporting & Hospital Transfer

41. How do we report incidents and Serious Adverse Events (SAEs)? What are the procedures around hospital transfer?

Please refer to Guidance Sheet 6 Safety Incident Reporting, 7A Hospital Transfer and 7B Continuing Care sites for further details.

Site Set Up & Funding Arrangements

42. How do I register interest in the study?

Please email surfon@npeu.ox.ac.uk to register your interest and we will send a feasibility form for completion. Once the site has completed feasibility assessment, we will get in touch to initiate site set up process. Please note that it is important to involve all key members during this stage (PI, lead RN, research tem, R&D, Pharmacy team, Contracts team).

43. What happens after site feasibility assessment?

Local Information Packs (LIPs) will be sent to sites and the SurfON study team will work with site to confirm capacity & capability to proceed to site set up.

44. When will the Site Initiation Visit (SIV) take place?

As part of the site set up process, SIVs will be conducted remotely via MS Teams.

45. What are the other training requirements?

Site staff will also need to complete Randomisation website and OpenClinica (study database) training online along with SIV.

46. Can I use the training materials for online self-training?

No, once the PI has received SurfON study training from the SurfON study team, the PI is then able to train other staff members or delegate this responsibility to another member who has received SurfON study training. All training will be fully documented within the ISF using the Training Log and a full audit trail of study activity will be maintained.

47. What materials will we receive as a site?

SurfON Site Documents Box containing ISF, Data collection File along with all study related documents will be sent to the sites around the time of SIV. This is provided along with SurfON Banner. Sites can reorder supplies anytime by getting in touch with the SurfON study team.

48. Are the key documents available online on SurfON website?

Our website is routinely updated and contains all essential documents, training materials, guidance sheets etc. related to the study. Some quick links are provided below:

- SurfON Protocol - https://www.npeu.ox.ac.uk/surfon/clinicians
- SurfON PIL - https://www.npeu.ox.ac.uk/surfon/parents
- SurfON Guidance Sheets - https://www.npeu.ox.ac.uk/surfon/clinicians/guidance-sheets
- SurfON Training Materials - https://www.npeu.ox.ac.uk/surfon/clinicians/training-materials
- SurfON Data Collection Forms - https://www.npeu.ox.ac.uk/surfon/clinicians/data-collection-forms
- Recruitment information - https://www.npeu.ox.ac.uk/surfon/recruitment

- Latest news - https://www.npeu.ox.ac.uk/surfon/whats-new

49. How does the mNCA (contract) get signed off?

SurfON mCNA is a tri-partite agreement. In line with agreement with Sponsor and local NPEU CTU, University of Oxford SOP, secure verified e-signatures can only be initiated directly by the SurfON study team.

We request sites to complete payment details on the mNCA and review the document for agreement. Once reviewed, we request sites to confirm *direct work email address* for the authorised signatory.

Please note that we cannot send signature request to generic inboxes in order to comply with audit requirements.

However, we can copy generic inboxes and other relevant team members to receive a final copy of the Fully Executed (FE) mNCA.

50. How do the sites get paid for recruitment? Could you clarify details around accrual funding for the site?

Under the model Non-Commercial Agreement (mNCA) signed for SurfON Per Participant Payment (PPP) will be provided to the site by the SurfON study team for each participant. Please note that this *only* applies to infant participation.

For sites in England, recruitment will be loaded via your site Local Portfolio Management System, such as Edge. It is the site's responsibility to maintain this data on the NIHR Central Portfolio Management System (CPMS). For more information, please go to https://www.nihr.ac.uk/documents/integrated-research-intelligence-system/11634. Each Local CRN (LCRN) will allocate funding to the member trusts based on their local arrangements and your local R&D should be able to clarify any further queries. For Scotland, Wales and Northern Ireland, please query this with your local R&D for further information.

51. Are Excess Treatment Costs (ETCs) arising from surfactant administration covered?

Yes, ETCs are covered for SurfON once the trust reaches their ETC threshold for the financial year, as confirmed by the ETC Assurance letter provided by the Specialised Commissioning Group. Therefore, where applicable ETCs will be paid to all infants regardless of the treatment arm they are randomised to. Further details from the letter are stated below:

Under national assurance arrangements established in October 2018, it has been agreed that when potential excess treatment costs relating to specialised care are identified in a research proposal, NHS England will have the opportunity to assure the costs proposed, consider whether expenditure might fall differentially across the country to inform regional budget setting and forecasting, and identify any issues or risks to be mitigated.

NHS England has now completed its review, based on the information received in the research proposal and the submitted SoECAT.

The completion of the financial assurance undertaken confirms that the only additional cost over and above standard of care relates to the surfactant and its prescribing costs which are usually covered within NHS tariff. However, as the study will not generate additional activity at the applicable tariff, we are content these costs are payable over and above normal NHS contract arrangements.

The gross and net (payable) excess treatment costs are therefore noted as the same figure in this case, at £844,328.50, payable retrospectively at the rate of £554.75 per patient recruited.

This information will be shared with NHS England's regional commissioning teams / hubs and this letter may be used by the principal investigator to demonstrate that the financial assurance of any additional costs or savings has been completed from a commissioning perspective.

52. Will there be any additional funding?

The study is fully NIHR portfolio adopted. Please note that in preparation for a potential extension to the study we have now changed our payment schedule from 0.1 FTE Nurse payment to PPP. As a site, where applicable ETCs will be paid for infants recruited as explained above.

53. How do we complete the SurfON Site Delegation Log?

The log is provided in the Site Documents Box. We request sites to carefully follow instructions provided within the log and list staff members using the correct responsibility codes and be signed off by the PI before conducting any study related activities.

We request all sites to use SurfON Site_Delegation Log V4.0_22nd March 2022 and supersede any previous versions. All staff members must be signed on the current delegation log and be signed off by the PI prior to conducting study activities.

54. How do the sites obtain Sponsor Green Light to begin recruitment?

Once the site set up process (SIV, Randomisation website and OpenClinica training, mNCA exchange, Delegation log completion, CV GCP submission (for PI, lead RN, Associate PI or Co-PI only), Local PI Protocol sign off, regulatory approvals for site, R&D confirmation of local C&C) , Sponsor Green Light will be provided.