Guidance Sheet 8:

Withdrawal and Unblinding

Centre for Trials Research
Canolfan Ymchwil Treialon

Withdrawal

- Staff can withdraw a baby from the BALLOON trial or discontinue BALLOON IMP at any time if parents wish or if it is deemed necessary for the baby's treatment.
- Parents do not have to give a reason for withdrawing a baby. Please ensure that you ask if:
  - The parents wish for their child to continue receiving Bactek.
  - The parents wish to continue completing questionnaires completed via the Trial App.
  - The parents agree that data can continue to be collected from the medical records.
  - The parents wish to continue taking swabs.
  - The parents agree that unprocessed samples (swabs) already collected can be used to answer the research question.
  - The parents agree that samples (swabs) already collected can be used for future research.
  - The parents agree that they are willing to attend any additional follow up visits as part of the trial.
  - The parents agree that they are willing to complete the questionnaires related to the trial.
  - The parents agree for blood sample collection to continue.
  - The parents agree to continue to donate samples (blood) for future research.
  - The parents wish to withdraw consent to all of the above.
- The time and date at which the baby was withdrawn from the clinical trial or the intervention discontinued should be documented in the baby's medical notes, together with any other necessary information.

  The withdrawal of consent shall not affect the trial activities already carried out and the use of data collected prior to participant withdrawal. The use of the data

collected prior to withdrawal of consent is based on informed consent before its withdrawal.

Participants lost to follow up or unable to complete withdrawal form

In the event a withdrawal form is not completed, it must be assumed that the parent(s)/guardian(s) withdraw their infant from all aspects of the trial. However, the information and consent form will state that any unprocessed viral swab samples will still be used. In respect of sub-study samples, these must be disposed unless the parent(s)/guardian(s) have signed the optional statement in the consent form that allows the samples to be retained in the event the parent(s)/guardian(s) do not complete the withdrawal form.

Withdrawal for medical reasons

If a participant is withdrawn for medical reasons by a clinician, the withdrawal form does not need to be completed. However, confirmation would be needed that the parent(s)/guardian(s) agrees to their infant's samples being retained and used as per original consent.

Furthermore, it is important to collect safety data ongoing at the time of withdrawal, especially if the participant withdraws because of a safety event. There is specific guidance on this contained in the Participant Information Sheet but briefly:

If a participant wishes to fully withdraw from the trial they will need to be assessed for a final safety assessment. If the participant is suffering a serious adverse reaction to the trial treatment when are withdrawn, their research team will be required to continue to collect information about that reaction until the adverse reaction has resolved.

An infant may be withdrawn or be withdrawn from trial treatment for the following reasons:

- Intolerance to trial medication
- Any alteration in the infant's condition which justifies the discontinuation of the treatment in the Investigator's opinion
- Non-adherence

Death of a Participant

If the death of a participant is reported to the recruiting site or the site discover a participant has died, then it is the responsibility of the site to complete the following steps:

- A SAE form must be completed and returned following the guidance in BALLOON Guidance sheet 7.
- Please notify the BALLOON Study Team at the CTR in Cardiff via a secure method.
- Please stop the App sending any further notifications or reminders to the parents/guardians.
- Please contact the parents/guardians when it is appropriate to do so and in a sensitive way to arrange to collect the sprays.

IN ALL INSTANCES WHERE A PARTICIPANT IS NO LONGER CONTINUING TO TAKE BACTEK PLEASE TRY AND OBTAIN ANY SPRAYS THE PARENTS/GUARDIANS STILL HAVE

Emergency Unblinding

- Emergency unblinding should only be carried out if the clinician carrying out the unblinding procedure is certain that:

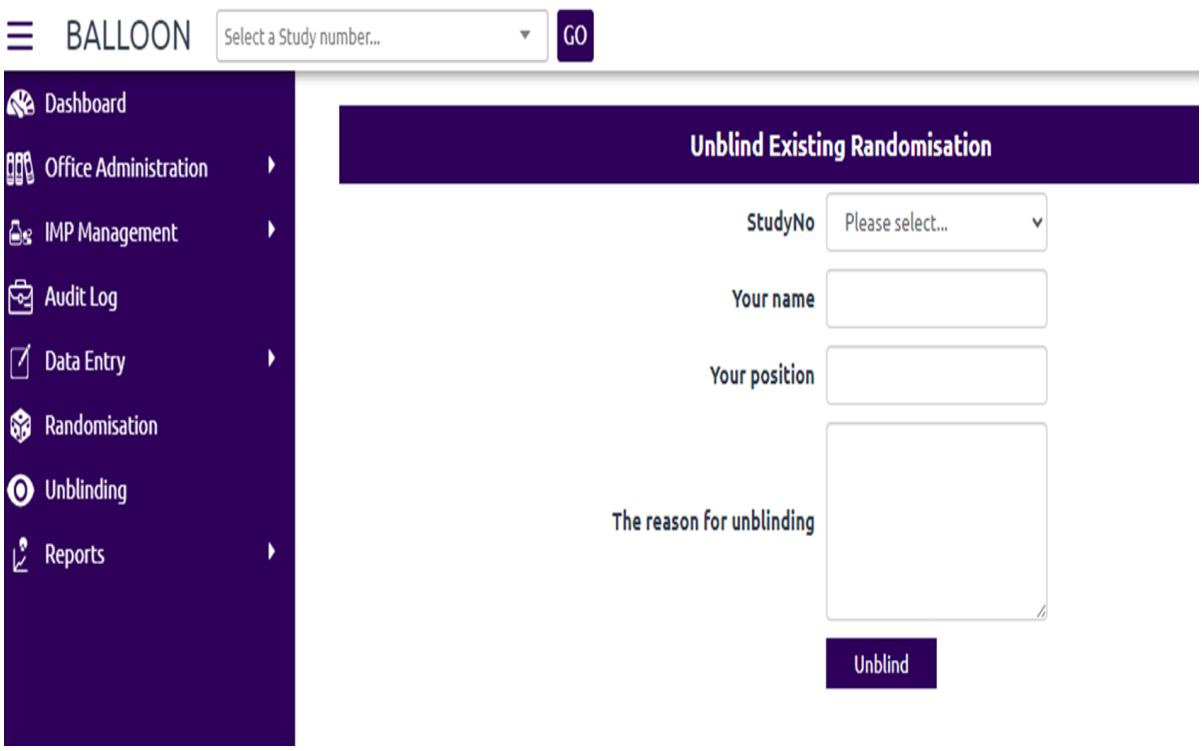
A. This is a **genuine emergency** AND

B. Knowledge of the treatment allocation (either Bactek or placebo) is **necessary to guide the clinical management of the participant**.

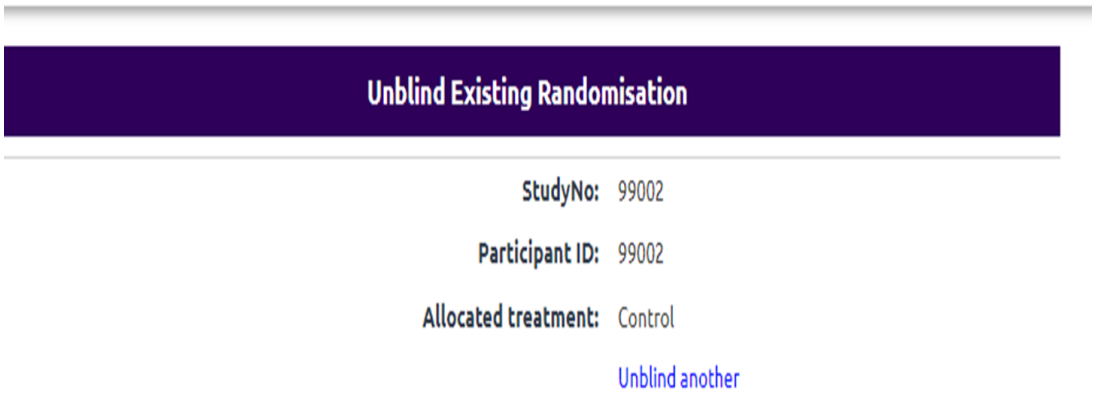
- Appropriate clinical management will be possible in the majority of cases without the need for unblinding by treating the participant as though they have received Bactek.

Web- based procedure for emergency unblinding:

- Emergency unblinding must be conducted by a medically qualified individual who is named on the delegation log
- During office hours (Monday-Friday 09:00-17:00), an attempt should be made to contact the Chief Investigator or designated clinical reviewer via the CTR BALLOON@cardiff.ac.uk to discuss the circumstances under which unblinding is being considered.
- An **Unblinding CRF** should be completed prior to conducting unblinding, where possible
- You will have been given a sealed envelope containing the following information:
- BALLOON randomisation website address
- Single-use login details and password
- Please login
- Click the three lines in the top left corner and then unblinding and complete the form. Take care to enter the correct CHaRT study ID.



- The system will then reveal the arm allocation of the infant- **knowledge of the allocation** should be strictly limited to those individuals who need to know for guiding the clinical management of the baby



- After the unblinding procedure is completed, please email the **Unblinding CRF** to the CTR as instructed on the form
- The BALLOON Trial Team will be automatically informed of any cases of unblinding.

Back-up procedure for emergency unblinding:

- In the event the randomisation website cannot be accessed (e.g. issues with login details or access to the website), CTR can be contacted during office hours (Monday-Friday 09:00-17:00) to perform unblinding on behalf of a site

- Contact the pharmacovigilance and safety team on, CTR-Safety@Cardiff.ac.uk with the particulars of the request, **including the baby's Study ID.** Please note that the team may wish to facilitate a discussion with the Chief Investigator or designated clinical reviewer prior to actioning the request

- The treatment allocation of the baby will be transmitted to a named induvial at site using a password protected email- **knowledge of the allocation** should be strictly limited to those individuals who need to know for guiding the clinical management of the baby