SOP for Fluenz and Saline Placebo Administration

FluSNIFF-Toddler Trial

Version: 3

Date: 25th September 2025

Applies to: All delegated site staff listed on the Delegation Log

Preamble: Importance of Maintaining Parent Blinding

In the FluSNIFF-toddler trial, the child's parent/guardian must remain blinded to whether their child receives the live attenuated influenza vaccine (LAIV) or saline placebo at each visit.

Why this matters:

- The primary outcome is whether a child experiences medically attended wheeze within 28 days of vaccination.
- If parents knew (or suspected) whether their child received a vaccine or placebo, it could influence how quickly or how often they seek medical care.
- This would introduce bias into the study results, making the data unreliable.

What sites must do:

- Always administer the spray in a way that prevents the parent from seeing which product is used.
- Ask parents to look away or focus only on holding their child during administration.
- Use identical wording and tone regardless of whether vaccine or placebo is given.
- Record and report any instance where unblinding occurs as a protocol deviation.

Maintaining blinding is essential for trial validity and ensures the results can be trusted to inform national vaccine policy.

1. Purpose

To describe the standardised procedure for administering the LAIV vaccine or saline placebo intranasally while maintaining blinding of the parent/guardian, in accordance with FluSNIFF Protocol v2.0.

2. Scope

This SOP applies to all clinical staff administering investigational products (Fluenz / LAIV/LIV or 0.9% saline placebo) during trial visits at participating sites.

3. Responsibilities

- Principal Investigator (PI): Ensures compliance with protocol and delegation of appropriately trained staff.
- Delegated Staff: Administer placebo/vaccine, maintain parent blinding, document administration in eCRF, and report any deviations.

4. Definitions

- **IMP:** Investigational Medicinal Product (**Fluenz**).
- **Placebo:** 0.9% saline administered intranasally using a syringe with nasal atomiser. The total dose is **0.2 ml** — approx. **0.1 ml per nostril**, the same volume and technique as the LAIV (Fluenz) spray.

5. Procedure

a. Preparation

- Prepare the saline placebo in advance of the visit.
- Use a clean tray, covered with a paper towel or second tray, to ensure the contents remain concealed when moving from refrigerator to administer the dose.
- All preparation must be carried out away from the parent/guardian's view.
- Perform hand hygiene and don gloves.

- **Saline placebo:**
  - Draw up 0.2ml of 0.9% saline into a 1ml syringe.
  - Remove the atomiser device from its outer packaging and apply to the end of the 1ml syringe.
  - Place in a second prepared tray, then cover to ensure concealment.

- Place the saline placebo dose(s) in the tray in the same refrigerator as the LAIV (so that the temperature of vaccine and placebo are the same at the point of adminstration; and to avoid parents being unblinded by differences between visits 1 and 2).

- **Fluenz:**
  - Remove Fluenz from the refrigerator
  - **Do not** shake the device.
  - Check for integrity (no leaks, cracks or discolouration).
  - Check expiry date.
  - Place in the prepared tray, covered to ensure concealment.

- Verify randomisation in the uMed eCRF.

b. Parent and Child Positioning

- Ensure the parent is facing away from the preparation area of the placebo and/or LAIV (or away from the refrigerator if in the same room).
- Remove the placebo or LAIV from the refrigerator and place in the prepared covered tray.
- Seat child on parent's lap facing to the side (not facing forwards) towards the person administering the placebo/LAIV, with parent holding child securely.
- The parent should put one arm around the child's torso and arms, and use the other hand on the forehead to gently steady them and limit movement.
- Ask the parent to "look over their shoulder" - this should be the opposite shoulder to the vaccinator during administration.
- Ask the parent to close their eyes during administration.
- Approach the child from the opposite side from where the parent has turned their head.
- Position vaccinator and child so the device is not visible to the parent.

Sample instructions:

"Please hold your child sideways on your lap with one arm around their body and the other hand on their forehead to keep them steady. While we give the spray, could you look over your shoulder, away from us, and close your eyes? This helps keep you blinded to what's given, which is important for keeping the study fair and reliable."

c. Administration

- Ensure you use consistent language for both the saline placebo and Fluenz nasal spray: 'Your child will receive a small nasal spray in each nostril. They can breathe normally.'
- **Saline placebo**:
  - Place tip of atomiser device just inside the nostril (do not insert deeply, do not apply firm pressure).
  - Depress syringe plunger to deliver approximately half of dose (0.1ml) into the first nostril.
  - Repeat procedure for the second nostril to deliver the complete dose.
- **Fluenz:**
  - Remove tip protector from sprayer. Do not remove dose-divider clip.
  - Place tip just inside nostril (do not insert deeply).
  - Depress plunger with a single motion as rapidly as possible up to the dose divider clip to administer 0.1ml to the first nostril.
  - Pinch and remove the dose divider clip from the plunger.
  - Spray remaining dose (0.1ml) into the second nostril) with the same technique.

d. Post-Administration

- Offer tissue paper if mild leakage occurs (do not wipe inside nose).
- Dispose of devices according to local sharps/waste policy. It is recommended that the nurse keeps a small sharps bin beside them, so the device can be disposed of immediately before the parent/guardian is asked to look back.
- Remove gloves and perform hand hygiene.
- Observe child per protocol for immediate adverse reactions.

e. Documentation

- LAIV: record batch/expiry in eCRF.
- Saline: record administration only (no batch required).
- Update IMP accountability log.

Electronic Medical Record (EHR/EMR) Entry: To maintain study blinding and avoid influencing clinical behaviour, no contemporaneous entry should be made in the participant's NHS Electronic Health Record (EHR) on the day of vaccination. All documentation of vaccine or placebo administration should be

entered into the EHR **on or after Day 57 (or later)**, once the final remote follow-up (Visit 3) has been completed, in line with the FluSNIFF EHR Guidance SOP.

f. Maintaining Blinding

- Ensure the parent's line of sight is blocked.
- Ask parents to look away during administration.
- Standardise staff behaviour regardless of product.
- Any accidental unblinding = protocol deviation (report immediately).

6. Training

- All delegated staff must receive training on this SOP during the Site Initiation Visit (SIV).

7. What to do if a parent is unblinded

If a parent becomes (or believes they've become) unblinded, that **doesn't automatically require withdrawal**. Do the following:

1. **Confirm ongoing consent.** Check the parent/guardian is happy to continue and document this in the eCRF - Consent Notes section.
2. **Treat as a protocol deviation.** Record the date/time, how the unblinding happened, and who was present; **notify Sponsor/CI** promptly.
3. **Continue per schedule.** Complete all remaining visits, eCRFs, and follow-ups exactly as planned unless there's a safety reason to stop or the parent withdraws.
4. **Do not attempt to re-blind.** Keep staff behaviour and phrasing identical going forward.
5. **Flag for analysis.** Ensure the CTU/statistician is notified so they can pre-specify handling (e.g., ITT includes all data; sensitivity/per-protocol may censor or adjust post-unblinding periods).
6. **Escalate only if clinical need.** If unblinding occurred for safety/clinical management, prioritise care and document the code-break pathway.

8. References

- FluSNIFF Protocol v2.0 (14 Aug 2025)
- FluSNIFF IMP Management Plan
- ICH-GCP E6(R2)