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FluSNIFF-toddler Study - Site Initiation Visit (SIV)

FUNDED BY
NIHR | National Institute for Health and Care Research

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Agenda

- Welcome & Introductions
- Study Overview
- uMed / Site responsibilities
- Parent/Child Journey
- About LAIV, Administration & Blinding
- GCP Introduction & Historical Context
- Key GCP Principles for FluSNIFF
- Consent, Delegation, IMP Management, Safety Reporting & eCRF Use
- Good vs Bad GCP Practice
- GCP Responsibilities for Nurses & AHPs
- GCP Case Scenario - group discussion
- uMed Platform & Data Entry
- Electronic ISF
- Archiving & Data Retention
- GDPR
- Q&A and Final Discussion

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Main Study Overview

- Phase 2 randomised single blinded placebo-controlled crossover trial assessing LAIV safety in children aged 12–23 months
  - Early Vaccine Group - Fluenz at Day 0
  - Late Vaccine Group - Fluenz at Day 28
  - Placebo at other visits
  - Parents / legal guardians blinded
- Sponsored by University Hospital Southampton, funded and supported by NIHR and RCGP RSC
- Delivery supported by uMed, a clinical research technology platform
- Primary outcome: Medically attended wheeze within 28 days

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uMed Responsibilities

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- Patient identification via EHR and outreach (site approves patients for outreach)
- Digital pre-screening and eConsent (obtaining parent signature prior to 1st Site Visit)
- Follow-up surveys (Day 7, 14 post-vaccine & Day 28 & 56)
- EHR data collection
- SAE alerting

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Site Responsibilities

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Arranging of 2 appointments

Conduct Visit 1 / Day 0

- Review and countersign eConsent
- Randomise
- First administration - Fluenz or placebo
- Provide instructions for surveys – parent reminder card!

A Site Guide will be provided!

Conduct Visit 2 / Day 28 (-3/+7)

- Re-confirm consent
- Second administration - opposite of first visit
- Provide instructions for surveys

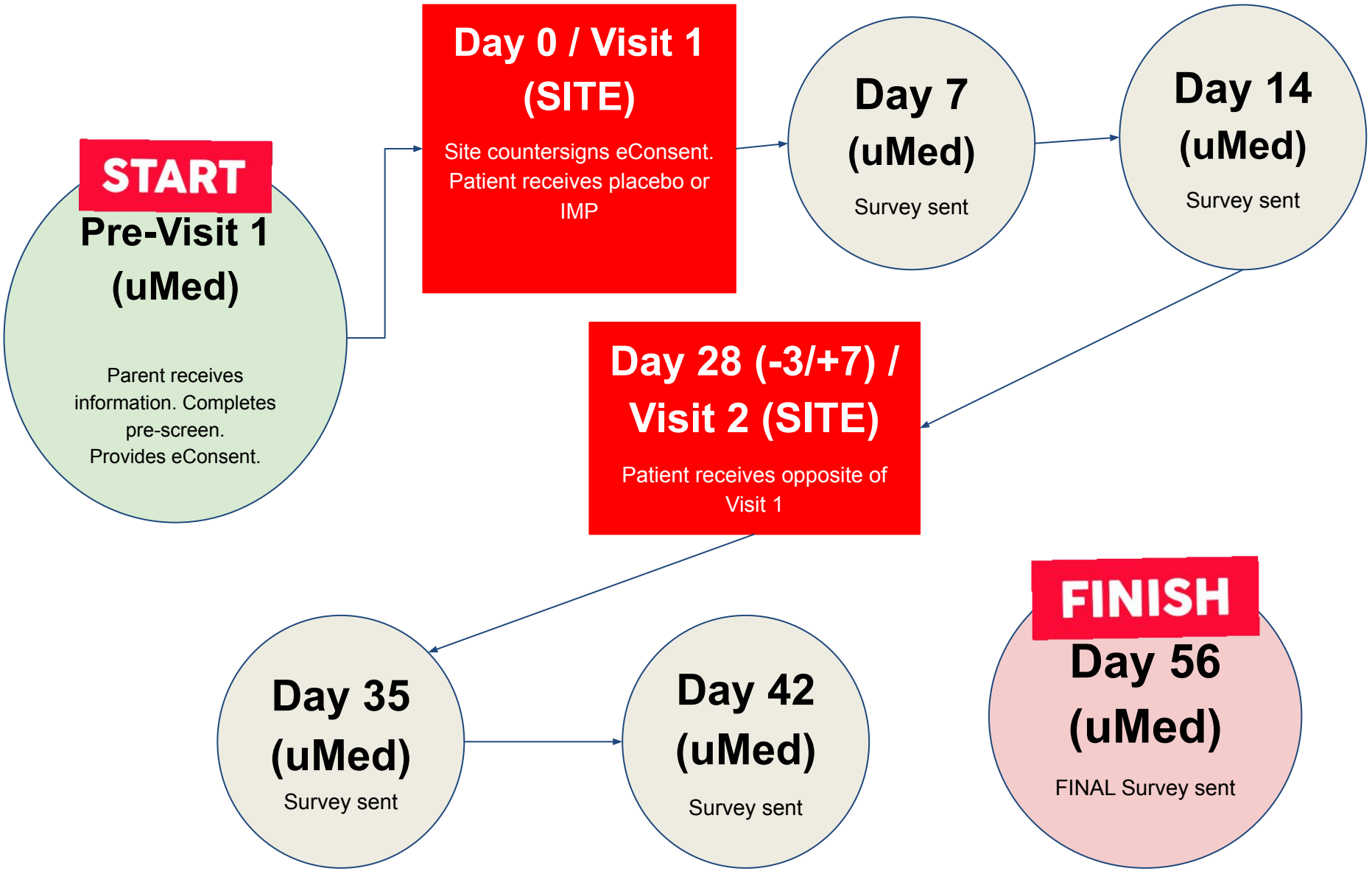
Complete visit data in uMed platform including recording IMP administration, batch, expiry

Confirm and record any SAE alerts received from uMed

Complete delegation log

Overview of journey

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LAIV & PLACEBO

What is LAIV?

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LAIV (Live Attenuated Influenza Vaccine), specifically **Fluenz**, is delivered **intranasally** — as a **nasal spray**.

- A small amount of vaccine is sprayed into **each nostril** - 0.2 mL total dose (0.1 mL per nostril) - using a prefilled single-use applicator (**needle-free)**.
- The child can breathe normally during administration; **no inhalation or deep breathing is required**.
- This method allows the weakened influenza virus to stimulate an immune response in the nasal passages, which is a natural entry point for flu infection.
- Ordered via UKHSA in usual way - free of charge!

Placebo

- 0.9% saline administered intranasally using a 1ml syringe with nasal atomiser. The total dose is 0.2 ml — 0.1 ml per nostril, the same volume and technique as the LAIV (Fluenz) spray.

What do these look like?



Atomiser



Syringe 1ml



Fluenz

Importance of Maintaining Parent Blinding

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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.

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.

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

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IMP Management

Parameter	Fluenz (LAIV)	0.9% Saline Nasal Spray
Source	NHS supply via UKHSA (ImmForm)	Routine stock vials/ampoules
IMP Status	Not IMP until removed from fridge for use	Not applicable
Storage	2–8°C, NHS cold chain protocols	Room temperature
Cold Chain Monitoring	NHS fridge logs until point of use	Not applicable
Accountability Log	Batch/expiry recorded at administration only	Not applicable
Transport	Handled via NHS processes	Not applicable
Packaging	Original NHS packaging	Original NHS packaging
Disposal/Return	Record used doses; discard per NHS SOP	Dispose per normal NHS procedures

WHAT IS AN MAAE / SAE

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MAAE – Medically Attended Adverse Event

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- New or worsening symptom requiring healthcare contact
- Includes GP, urgent care, A&E, or telephone consultation
- **Primary Outcome** = wheeze within 28 days

SAE – Serious Adverse Event

❌

- Death or life-threatening event
- Hospitalisation or prolonged stay
- Significant disability/incapacity
- **Must be reported within 24 hours** of site awareness

📌 **In FluSNIFF:** Parents report via uMed surveys → Sites are alerted to confirm and complete reporting.

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SAE & MAAE Reporting

- MAAEs or SAEs reported by parents via uMed at Days 7, 14 post-vaccine and Days 28 & 56
- Sites alerted by uMed to any potential SAEs
- Site must contact family to confirm details and complete SAE form
- SAEs must be reported within 24 hours of becoming aware
- All SAEs handled within uMed platform with oversight by CI/Sponsor

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💻 Let's take a look at the platform…

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…and walk through a **patient's data entry journey** at site.

We'll cover:

- How to log a Visit Date when booked and change
- How eConsent is countersigned at site
- How to randomise
- What data is entered at each site visit
- Where sites can view and update study information
- How Serious Adverse Events (SAEs) are reported

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Electronic Investigator Site File (eISF)

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📁 What is the eISF

FLORENCE is an electronic Investigator Site File (eISF) which is a secure digital platform for storing and managing all essential study documentation.

Is it accredited? Yes, Florence is compliant to EU Annex 11, Certified 21 CFR Part 11, ICH GCP, GDPR, HIPAA, ACIPA

Is there training provided? Training is provided and can be access via eISF Training for Study Staff. Once completed you will gain a certificate.

How to get access? Access will be provided by the Site Admin, who will be discussed with UHS as the Sponsor.

Who to contact if there is a problem? Please email florenceadmin@uhs.nhs.uk

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Archiving and Data Retention

Consent and identifiable data to be stored securely for 25 years

Data Protection – Your Role Under GDPR

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🛡️ **Data Protection Responsibilities**

- Handle all participant data in accordance with GDPR
- Only access data you're authorised to see
- Never share login credentials to uMed or any platform

🔐 **eConsent & eCRF Data**

- Personal data collected by uMed must be securely stored
- Any paper backup must be securely locked and uploaded as needed

💡 **Always report data breaches or concerns immediately to the PI or study team.**

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GCP Guidance

- Targeted GCP included in this SIV for those without formal training
- NIHR certification encouraged NIHR Learn
- PI must ensure all staff are trained and supervised
- Training records must be filed in the eISF
- Contact study team for additional training resources

What is GCP?



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Good Clinical Practice (GCP) is an internationally recognised standard that ensures the **rights, safety, and well-being of clinical trial participants** are protected, and that the **data collected are credible and accurate**.

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Let's break down the historical context that led to the development of GCP

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In the past, some research studies involved unethical practices that put human subjects at risk. Two notable examples:

- **Tuskegee Syphilis Study (1932–72)**: In this study, African American men with syphilis were left untreated, even after effective treatments became available. Researchers prioritized studying the disease's progression over providing proper care.
- **Nazi Experiments (1933–45)**: During World War II, Nazi doctors conducted inhumane experiments on prisoners in concentration camps where people were forced to undergo horrific harm or death, including testing the effects of torture and disease.

Ethical Response

- **Nuremberg Code (1947)** & **Declaration of Helsinki (1964)**: Established principles of **informed consent** and **participant protection**.

Why GCP Was Created

- Addressed **inconsistent trial conduct** and **participant safety concerns**
- Ensures **rights, safety, and well-being** of participants
- Promotes **high-quality, reliable research data**

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Informed Consent

- Parent/guardian completes eConsent via uMed prior to Visit 1
- Site must confirm consent at first visit and countersign
- Allow time for questions; ensure understanding and voluntariness
- Consent must be documented before any procedures
- Nurses/AHPs may confirm and countersign eConsent **only if trained and delegated**.
- Paper ICF available as backup if needed

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Delegation of Duties

- Only delegated staff (on log signed by PI) can perform study tasks
- Roles must match training and be recorded in the Delegation Log
- Log must be kept current and stored in Investigator Site File (ISF)
- PI remains ultimately responsible for oversight and compliance

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Good vs Bad GCP Practice (FluSNIFF Context)

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GCP Area	✅ Good Practice	❌ Bad Practice
Informed Consent	Site staff confirms and countersigns eConsent before any procedures start	Proceeding with dosing before confirming eConsent
Delegation of Duties	Only staff on the Delegation Log (signed by PI) perform study tasks	New team member performs randomisation without being added to the Delegation Log
Protocol Adherence	Follows randomisation schedule for dosing exactly as per protocol	Administering vaccine outside visit window without documenting deviation
Data Entry (uMed eCRF)	Enters all data on the same day using verified source information	Data is entered days later from memory or notes
IMP Accountability	Batch number and expiry date recorded immediately after dosing	Forgets to record batch details or updates them later from packaging
Safety Reporting (SAEs)	Follows up on uMed alerts and reports SAE within 24 hours	Ignores alert assuming it's minor; no follow-up with family
Document Management	Files all signed logs in eISF or uploads clear scans	Leaves signed logs in drawers or skips upload to eISF

Why GCP Matters: Patient Safety First

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- GCP is not just about compliance – it's about protection.
- Children aged 12–23 months are a vulnerable group.
- GCP ensures:

- Informed parental consent is valid and voluntary
- Safe vaccine handling and dosing
- Proper reporting of any adverse events
- Accurate records for every visit

Every action taken under GCP protects the child's rights, well-being, and safety.

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Questions & Key Contacts

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Study team and uMed contact details provided in Site Guide

Any further queries?

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