UNIVERSITY OF LEEDS

The Leeds Teaching Hospitals NHS
NHS Trust

Consent and Eligibility Guidance for Clinical Trials (of an Investigational Medicinal Product)

1) Why is documenting consent and eligibility important?

"If it isn't documented, it didn't happen"

In order to demonstrate that all trial participants were **fully consented prior to any trial-related activity** and to evidence participants were **confirmed as eligible for inclusion in the trial prior to dosing**, the steps taken to obtain informed consent and confirm eligibility must be fully documented at source[a] **and** on the Case Report Form (CRF).

2) Why is it relevant to me and my study?

As Chief / Principal Investigator for a UoL / LTHT Sponsored trial, it is your responsibility to ensure that the approved consent process is followed at site and that eligibility is reviewed and confirmed in accordance with the principles of Good Clinical Practice (GCP) and your approved trial Protocol.

3) What do the MHRA look for in an inspection?

When reviewing source data[b] and the CRFs for your trial participants, the MHRA will be looking to be able to **fully reconstruct** their participation throughout the trial, from the point they were initially approached, all the way to the end of their participation.

In order to fully document consent and eligibility, the participants' medical records must contain **all trial-related documentation** (e.g. participant information sheets, signed consent forms, protocol-required screening data, etc.) and must document **all events** related to consent and eligibility (e.g. consent discussions, evidence of review of screening results, etc.).

The MHRA will also expect to see all protocol-required data documented at both source **and** on the CRF i.e. eligibility must be confirmed by a medically qualified doctor in **both** places.

4) Documenting the consent process

What are examples of best practice? *

- ✓ Document when the participant was first approached and the date the Participant Information Sheet (PIS) was provided (this helps to demonstrate that the participant had ample time to consider the trial)
- ✓ Fully document every step taken to obtain consent at source (e.g. via direct annotations in the medical notes) e.g. **what** happened, **when** it happened, **who** was involved.
- ✓ If you are planning on obtaining informed consent, ensure you are authorised and delegated to do so on the delegation log, and have up-to-date GCP training (i.e. dated within 2 years)
- ✓ Ensure all related documentation is fully complete and filed at source and in the ISF/TMF as applicable.
- ✓ Consent forms must be signed by the person obtaining consent and the patient in real time **on the same date.**
- ✓ The participant must **personally** sign **AND** date their section of the form.
- ✓ Document continued consent at each trial visit.
- ✓ Informed consent is an on-going process and therefore any changes to trial design, medications, or trial risks may require re-consent from participants. Where required, re-consent should be done in a timely manner, usually at the next protocol-defined visit.

Common consent related monitoring findings include:

- ✘ *Initial provision of PIS to participant and subsequent consent process not fully documented at source (e.g. when patient was approached, evidence of consent discussion, version/dates of PIS and date ICF signed, etc.).*
- ✘ *Copies of PIS and signed ICF not filed at source and in the ISF/TMF.*
- ✘ *Informed consent obtained by individuals not authorised and/or not delegated to do so.*
- ✘ *No evidence of continued consent being obtained from the participant at every trial visit.*
- ✘ *Use of an incorrect version of the PIS or ICF.*
- ✘ *Where appropriate, participants not re-consented to the most recent version of the PIS in a timely manner.*

*** Note:** *For full guidance on what must be documented for consent and eligibility, please refer to the 'LTU_QM23' SOP [(1)].*

5) Documenting review and confirmation of eligibility

What are examples of best practice?

- ✓ **The MHRA consider the decision of whether a participant is eligible for entry into a clinical trial to be a medical decision and therefore must be confirmed by a medically qualified doctor.**
- ✓ **Prior to dosing**, a statement of eligibility **MUST** be recorded at both source (e.g. via annotations in medical notes) **AND** on the CRF.
- ✓ This statement must confirm the results were within the acceptable protocol-defined ranges and that the patient meets **all of the inclusion criteria and none of the exclusion criteria.** The statement must be signed by an authorised and delegated **medically qualified doctor**.
- ✓ If the medical decision for entry is within the CRF, it must also be reflected in the participant's medical notes. However providing the CRF eligibility statement is **signed in real time by the medically qualified doctor,** the MHRA do allow the corresponding statement in the notes to be entered by a research nurse, providing it is clear the **decision** was made by a medically qualified doctor.
- ✓ Results for **all** protocol-required screening assessments must be filed at source and signed and dated by a medically qualified doctor to evidence clinical review, **prior** to dosing the patient.
- ✓ If it isn't feasible to print and file particular results (e.g. if there are a high volume of blood tests), a statement can be made in the medical notes documenting the review of the results against the inclusion/exclusion criteria by a medically qualified doctor.
- ✓ A patient must not be entered into a trial if they do not meet **all** of the eligibility criteria for the trial.

Common eligibility related monitoring findings include:

- ✘ *Eligibility confirmed by a medically qualified doctor on the CRF but not documented at source.*
- ✘ *No evidence of review of screening results by a medically qualified doctor prior to confirmation of eligibility (e.g. results not filed, or not signed and dated by the investigator, signatures dated after confirmation of eligibility).*
- ✘ *Participant enrolled onto a trial despite not meeting eligibility criteria i.e. a protocol waiver (see section 6).*

6) What happens if a patient doesn't exactly meet the eligibility criteria?

In the eyes of the MHRA, inclusion / exclusion criteria is defined in the trial protocol **to protect the safety of trial participants.** Therefore, entering a patient into a trial who doesn't fully meet the eligibility criteria is a **breach of GCP and may result in patient safety findings during inspections.**

Protocol waivers (approval given for a patient to enter a trial despite them not meeting one or more of the eligibility criteria) **are not acceptable** as they constitute a deliberate breach of Regulation 29 of SI 2004/1031, which states ***"no person must conduct a clinical trial otherwise than in accordance with the Protocol".***

How to avoid protocol waivers/deviations relating to eligibility:

- ✓ Review your inclusion/exclusion criteria to ensure there is no room for ambiguity or interpretation.
- ✓ If upon review any of the eligibility criteria require further clarification please submit an amendment to Sponsor QA for review *(for related guidance, please see the 'QCRES_03' SOP [(2)]*

- ✓ Monitor screen failures and continually assess the appropriateness of the protocol eligibility criteria.
- ✓ If as a CI you feel the protocol is too restrictive, submit an amendment request to Sponsor QA for review.
- ✓ Changes to eligibility criteria are always considered a substantial amendment and must have QA, MHRA, REC and HRA approval prior to implementation.
- ✓ Consult Sponsor QA and the CI/PI if in any doubt as to whether a patient should be enrolled.

Footnotes

[a] ***Source documents*** *are 'Original documents, data, and records' - ICH GCP [3] e.g.: hospital records, clinical and office charts, nursing notes, source data worksheets, etc.*

[b] ***Source data*** are contained within source documents and are defined as: *'All information in original records, and certificated copies of original records, of clinical findings, observations or other activities in a clinical trial necessary for the reconstruction and evaluation of the trial i.e.* ***where the data are first captured*** *(either written or electronically)'* - ICH GCP

Key Resources & Further Reading

[1] **LTU_QM23** A Researcher's Guide to Source Documentation [2] **QCRES_03** Researcher's Guide to Notification of Amendments for UoL LTHT Sponsored CTIMPs	*Sponsor QA (LTHT / UoL)*	http://lthweb.leedsth.nhs.uk/sites/research-and-development/research-and-development-homepage/quality-and-assurance
[3] **ICH Guideline for GCP E6 (Revision 2)**	*ICH*	*http://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/Guidelines/Efficacy/E6/E6_R2__Step_4.pdf*
[4] **Good Clinical Practice Guide**	*MHRA*	https://www.tsoshop.co.uk/MHRA/Good-Clinical-Practice-Guide/

* **Should you have any queries or concerns, or would like further information regarding the content of this bulletin, then please do not hesitate to contact the Sponsor Quality Assurance Office on Tel: 0113 30 60464** *