DIVISION OF RESEARCH AND INNOVATION

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Title: Dose Escalation	
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1. Scope

This SOP is applicable to

- All Great Ormond Street Hospital for Children (GOSH) or Institute of Child Health (ICH) staff who will be involved in the set-up and/or conduct of research studies that involve dose escalation.

Further to the requirements listed in this SOP, personnel must also comply with:

- Any additional study-specific requirements mandated by the PI, Sponsor or R&D.

2. Purpose

The purpose of this SOP is to outline the minimum requirements for performing studies that involve dose escalation.

3. Definitions/Abbreviations

Clinical Research – As per UK Framework for Health and Social Care Research and HRA/MRC 'Is my study research?' tool.

Dose escalation – The progressive increase in dose following the review of available data from the previous dose level(s).

4. Responsibilities

Duties may be delegated but the responsibility always remains with those listed.

4.1 The study Principal Investigator (PI) is responsible for:

- Ensuring that their study complies with the requirements detailed in this SOP.
- Ensuring that the dose escalation procedure is detailed in the protocol and/or Risk Assessment.
- Authorising the dose escalation decision (unless this is formally delegated to another suitably qualified investigator).
- Ensuring the dose escalation procedure is followed and appropriately documented in the Investigator Site File (ISF) and medical notes.

4.2 All staff are responsible for:

- Ensuring their practice meets the requirements of this SOP, the study protocol, GCP and any applicable legislation, policies, procedures or guidelines.

5. Procedure

For dose escalation studies, there must be a robust, clearly defined dose escalation procedure. This procedure must be followed and each step formally documented and filed in the Investigator Site File (ISF) and medical notes to demonstrate compliance and to allow for the reconstruction of the study.

5.1 Written Dose Escalation Procedure

The flowchart in Appendix 1 details the dose escalation stages and the minimum information that is required to be included within the written procedure at each stage. The procedure should be included in the protocol.

5.2 Dose Escalation

Dose escalation must follow the agreed procedure, unless this would be a risk to study participants (in this case contact the Joint R&D office IMMEDIATELY).

The dose escalation must not proceed if dose escalation limits are violated, unless an appropriate amendment receives the necessary approvals.

An amendment to the dose escalation procedure must have written approval from the Sponsor and appropriate authorities before it can be implemented.

5.3 Dose Escalation in the Absence of the PI (Delegation)

The PI may delegate this task to another suitably qualified investigator involved in the clinical study, but this delegation must be formally authorised and documented in the study delegation log before this individual performs the activity.

5.4 The Quality of Data Used to Make Dose Escalation Decisions

It is imperative that the data used to make the decision are accurate. Therefore, all data used for the dose escalation decision must be subject to quality control (QC) procedures and this QC must be documented. The PI must request clarification from the Sponsor that any data received from an external source (e.g. from the Sponsor or another NHS Trust) has also been quality controlled. If data is in a draft format, this must be clearly documented and justified and consideration given to the influence of this data on study decisions.

5.5 Dose Escalation Documentation and Compliance

The site file must contain and clearly reflect the data reviewed and the decisions taken. All dose escalation steps must be clearly documented and retained in the ISF in order to demonstrate compliance with the dose escalation procedure and this SOP. Dose escalation documentation will be subject to audit to ensure compliance with this SOP.

6. Related Documents

NA

7. References

- MHRA Good Clinical Practice Guide (Grey Guide)
- MHRA Phase I Accreditation Scheme Requirements
- MHRA Phase I Accreditation Scheme Guidance Document
- ABPI (2012) Guidelines for Phase I Clinical Studies
- ABPI (2011) First in Human Studies

8. Appendices

- Appendix 1: Minimum Information Required For Dose Escalation Process

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