NIHR Wellcome Trust Clinical Research Facility
Early Phase Safety Committee (EPSC) Terms of Reference

Purpose:
The Early Phase Safety Committee (EPSC) will convene to support the scientific review and clinical risk assessment of all Phase I and First in Human (FIH) studies that will be conducted within the Southampton NIHR Wellcome Trust Clinical Research Facility (CRF). Where the need is identified by the CRF Directors, the EPSC will also provide support for the scientific review and clinical risk assessment of other early phase studies.

The EPSC will share experience and expertise in the field of early phase studies to ensure that all Phase I and FIH studies that are conducted within the CRF have been risk assessed and associated contingency planning implemented.

Composition of the EPSC:
The EPSC will comprise individuals from both the Trust and the University of Southampton, and when needed external bodies with appropriate expertise in early phase studies, statistics, clinical pharmacology, toxicology and/or pharmacy.

Chair:	CRF Director or CRF Associate Director
Member:	UHS RG&QA Manager
Member:	SCBR QA Lead
Member:	Clinical Pharmacologist
Member:	Appropriate representation from Cancer Sciences
Member:	Appropriate representation from UHS Clinical Trials Pharmacy
Member:	Statistician
Member:	Other expertise as required

Representation from other areas of the Trust or University may be called to the EPSC with agreement of the group to discuss specific matters.

The committee members assessing a study must not have any involvement in the study under review or have any other conflicts of interest.

Terms of Reference:
For FIH studies (and any high risk early phase studies in that have been identified as requiring EPSC support), the risk assessment (with associated contingency plan) will be reviewed by the committee and signed off by the chair. The decision as to what constitutes 'high risk' will be made by the EPSC Chair or the study sponsor.

All other Phase I studies (and any early phase studies that have been identified as requiring EPSC support) will have the risk assessment (and associated contingency plan) reviewed by the CRF Director or CRF Associate Director. Advice will be sought from other members of the EPSC as appropriate, and 'Chairman's Action' will be used to sign off the risk assessment.

The EPSC will facilitate the following, as required:

- Provide a forum for members to share knowledge and expertise relating to investigational medicinal products (IMPs) proposed for specific early phase studies that will take place in the CRF.
- Review the curriculum vitae of the study Principal Investigator (PI) and any co-investigators for evidence of appropriate qualifications, relevant experience and the competency to supervise and conduct the study under review.
- Review and risk assess pre-clinical data of proposed Phase I studies from a technical and clinical risk perspective on a case by case basis.
- Risk assess all aspects of the IMP, including: class, novelty, species specificity, mode of action, potency, dose and concentration response relationship for efficacy and toxicity, and route of administration.
- Assess whether the trial should be submitted for review by the Expert Advisory Group (EAG) to the Committee of Human Medicines (CHM).
- Consider the probability and severity of adverse reactions relating to study drugs, and consider the availability of specific antidotes and appropriate supportive treatment.
- Assess procedures and any non-IMP used in the specific Phase I study under review.
- Consider whether the trial should involve healthy subjects or patients.
- Provide a decision on whether proposed studies are approved to take place in the CRF from a technical, scientific and clinical perspective.
- Establish and document necessary contingency plans for all aspects of the study that must be in place prior to the initiation of Phase I studies in the CRF. For example, starting dose, dose escalation, administration of doses, facilities and staff, procedures, and subject type.
- Review the impact of any protocol amendments and/or any new safety information during the study. Provide a decision on the acceptability of the changes within the context of the original risk assessment and contingency plan.

Quorum:
For FIH studies (and any high risk early phase studies in experimental medicine that have been identified as requiring EPSC support), the committee requires five members to be quorate. The quorum must include a Pharmacologist, (or other

appropriately qualified individual) the CRF Director / Associate Director and the UHS RG&QA Manager / SCBR QA Lead.

For all other Phase I studies (and any early phase studies that have been identified as requiring EPSC support), the risk assessment (and associated contingency plan) will be reviewed by the CRF Director or CRF Associate Director.

Secretariat:
Secretarial support (minutes) for face to face meetings will be provided by the SCBR QA Lead. Minutes will be distributed to all EPSC members following a meeting, and the minutes will be distributed to other individuals as necessary.

The agenda items for each face to face meeting will be collated by the SCBR QA Lead following discussion with the CRF Director or Associate Director. Agenda items will be distributed to all EPSC members prior to a meeting date.