CO-ENROLMENT POLICY

DOCUMENT NO.:	**POL008 v2.0**
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1 INTRODUCTION

1.1 The Academic & Clinical Central Office for Research & Development (ACCORD) is a joint office comprising clinical research management staff from NHS Lothian (NHSL) and the University of Edinburgh (UoE).

1.2 Co-enrolment is the process of entering participants into more than one study either concurrently or in some cases sequentially.

1.3 Failure to declare cases of co-enrolment may result in the Clinical Trial Liability insurance being invalid.

1.4 There are no direct statements regarding co-enrolment in the Medicines for Human Use (Clinical Trials) Act SI 2004/1031 (as amended) - transposed from EU Directive 2001/20/EC.

1.5 The Journal of the Intensive Care Society released an editorial (volume 4, number 2, April 2013) concerning co-enrolment. It described a number of issues that should be considered before co-enrolment is sanctioned. These issues included: study design and statistical considerations; legal and ethical considerations; biological and scientific rationale; participant considerations and; logistical and organisational issues.

1.6 A meeting of the National Research Ethics Advisors' Panel (10/July/2013) discussed co-enrolment and provided comment as follows:

- "Researchers should not place blanket restrictions on patients' freedom of action without justifiable reasons for doing so agreed with the REC."
- "RECs should look closely at any project that stipulates that participants should not take part in any other studies to assure themselves that any such restriction was necessary, primarily for participants' safety. This applies especially to studies involving long-term follow-up of participants."
- The panel agree that the washout period might vary depending on the trials involved but should always be clinically informed and justified.

2 SCOPE

2.1 This document is relevant to all researchers participating in or organising research studies sponsored by NHSL and/or UoE and hosted by NHSL.

2.2 This document is relevant to all members of ACCORD who facilitate, manage, co-ordinate or advise on clinical research sponsored by NHSL and/or UoE and hosted by NHSL.

2.3 This document is relevant to research where individual participant consent is taken.

3 POLICY

3.1 Considerations for Co-Enrolment

3.1.1 Co-enrolment will be considered and may be permitted in in compliance with the study protocol.

3.1.2 In all cases, the safety of study participants, interventions involved, participant burden and the potential impact on the study endpoints must be considered.

3.1.3 Trial-specific co-enrolment plans must be included in the protocol or clinical investigation plan for all regulated drug and device trials and should be considered on a case by case basis for non-regulated research.

3.1.4 For studies subject to a combined risk assessment as per ACCORD SOP GS002, details of proposed co-enrolment will be described and agreed as part of the risk assessment.

3.1.5 Details of co-enrolment may entail identifying specific studies with which co-enrolment will be permitted. Alternatively, there may be situations where generic circumstances can be described, defining when co-enrolment can be permitted. For example, co-enrolment could be permitted with studies that involve only the collection of data (e.g. questionnaires) or tissue samples (e.g. blood). If participant follow-up is required, consideration may need to be given as to whether the follow up outcome measures could be influenced by participation in other co-enrolling studies especially where they involve a trial intervention.

3.1.6 Interventional Trials

A washout period should be defined if there is an intention to allow co-enrolment between studies involving interventions. For CTIMPs, the Sponsor Representative(s) and Chief Investigator (CI) should consider seeking the opinion of a clinical pharmacologist, who is considered to be independent of both studies, regarding the length of a minimum wash-out period. Pharmacokinetic (absorption, distribution, metabolism and excretion) and pharmacodynamic (drug action including binding and interactions) effects

should be considered in such an assessment. Similar considerations should be made for other non-CTIMP pharmaceutical interventions as well as other non-pharmaceutical interventions such as diagnostic, radiation, device or surgical interventions.

3.1.7 Participant Burden

Overall burden to participants should be given due consideration by the Sponsor Representative(s) and CI, including the number of study visits involved, or follow up requirements e.g. participants completing questionnaires for multiple studies in the same or similar disease groups may present a risk of participant non-compliance due to burden and/or confusion over which questionnaires to complete.

3.1.8 Study Design and Outcomes

Consideration should be given to whether co-enrolment is likely to influence the outcome measures and end-points of the trials, or compromise the overall study design and delivery. Even for non-interventional observational studies where the outcomes may be questionnaire data, it is possible responses provided for one study may alter responses given in another study.

It is recommended that co-enrolment proposals be provided to statisticians representing each study, where a statistician has been identified, to determine if study outcomes could be affected.

Co-enrolment proposals should be provided to the Trial Steering Committee (TSC) Chair and/or Data Management Committee (DMC) Chair for each study, if one has been assembled or is intended to be assembled. The TSC/DMC Chair should consider any potential for co-enrolment to: compromise study design; affect study outcomes e.g. by introducing bias; adversely affect participant safety and; increase participant burden such that risk outweighs benefit. The TSC/DMC Chair should also consider the compatibility of both protocols e.g. ensure that eligibility criteria and prohibited concomitant medications cannot compromise co-enrolment plans and ensure that co-enrolment plans do not alter any expected/required enrolment distribution models.

3.2 Safeguards

3.2.1 First in Human and Phase I Trials

Co-enrolment will not be permitted for interventional or experimental studies where one or more of the studies concerned are classified as First-In-Human studies or a Phase I trial.

3.2.2 Clinical Trials of an Investigational Medicinal Product (CTIMPs)

Interventional Phase CTIMP-CTIMP Co-Enrolment

Enrolling a participant in the interventional phase of more than one CTIMP (i.e. a participant receiving IMP(s) from more than one trial concurrently) is not recommended. In such cases, the risk assessment will be appraised by the Sponsor Representative(s) as per SOP GS002 (Combined Risk Assessment) and the CTIMP-CTIMP Co-enrolment Checklist (POL008-F01) will be completed by the Sponsor Representative(s) in conjunction with the CI prior to the co-enrolment proceeding. The checklist and associated correspondence should be filed in the Trial Master File/Sponsor File.

In exceptional circumstances, a formal co-enrolment agreement may be required.

Follow-Up Phase CTIMP-CTIMP Co-Enrolment
In cases where participants are in long term follow-up (e.g. where follow-up data only is being collected) co-enrolment may be permitted. In such instances, the CTIMP-CTIMP Co-enrolment Checklist (POL008-F01) must be completed by the Sponsor Representative(s) in conjunction with the CI prior to the co-enrolment proceeding. Where necessary, the combined risk assessment may need to be appraised as per ACCORD SOP GS002 (Combined Risk Assessment).

CTIMP-NonCTIMP Co-Enrolment
Participants who are active in the interventional phase of a non-CTIMP can be co-enrolled to a CTIMP provided the CTIMP-nonCTIMP Co-enrolment Checklist (POL008-F02) is completed by the Sponsor Representative(s) in conjunction with the CI prior to the co-enrolment proceeding.

Co-enrolment with non-interventional research (e.g. sample only, questionnaire studies) will typically not require any formal documentation or authorisation from the Sponsor Representative(s).

3.2.3 Non-CTIMP Co-Enrolment

Arrangements for co-enrolment with another interventional non-CTIMP will be permitted in compliance with the study protocol. Written agreement in the form of email communication is required from both CIs and must include a statement on the impact on participant burden and study outcomes as a minimum.

Co-enrolment between non-interventional research (e.g. sample only, questionnaire studies) will typically not require any formal documentation or authorisation from the Sponsor Representative(s).

3.2.4 Co-Enrolment Agreement

In exceptional circumstances (e.g. at the request of Sponsor(s) and/or insurer(s)), proposals for co-enrolment between active CTIMPs may be required to be captured in a written, authorised agreement between the Sponsors and CIs of each trial. In addition, a copy of the protocol of a hosted

study co-enrolling with a study sponsored by NHSL and/or UoE must be provided to the Co-Sponsors.

The Co-Enrolment Agreement will be drafted by the UoE or NHSL contracts team as appropriate, at the request of the Sponsor Representative and/or the local Investigator.

The finalised agreement will be signed by the Sponsors and the CI of both CTIMPs involved.

3.2.5 Accidental/Unintentional Co-Enrolment Identified Retrospectively

It is recommended that systems are implemented by Investigators to prevent accidental/unintentional co-enrolment. Systems may include keeping a study record of all participants who have been co-enrolled and utilising shared patient information databases (e.g. TrakCare) to check on the enrolment status of a participant. Furthermore, it is recommended that Investigators routinely ask participants if they are enrolled in another study.

Incidents of accidental/unintentional co-enrolment must be reported to the Sponsor as a protocol deviation/violation, in accordance with SOP CR010 (Management of Protocol and GCP Deviations and Violations). Where cases of accidental/unintentional are identified, the Co-Sponsors will determine the appropriate course of action.

4 REFERENCES AND RELATED DOCUMENTS

- The Medicines for Human Use (Clinical Trials) Regulations (SI 2004 No. 1031), as amended.
- Editorial: the Journal of the Intensive Care Society, volume 4, number 2, April 2013.
- National Research Ethics Advisors' Panel meeting, 10/July/2013
- SOP CR010 Management of Protocol and GCP Deviations and Violations
- SOP GS002 Combined Risk Assessment
- POL008-F01 CTIMP-CTIMP Co-enrolment Checklist
- POL008-F02 CTIMP-nonCTIMP Co-enrolment Checklist

DOCUMENT HISTORY

Version Number	Effective Date	Reason for Change
1.0	12 JUL 2018	Co-enrolment guidelines (GL001) have been transferred to an ACCORD policy.
2.0	27 MAY 2022	Removal of notifying insurers of CTIMP-nonCTIMP co-enrolment from POL008-F02. Minor clarifications to text of SOP. Minor clarifications to POL008-F01 and POL008-F02 (both updated to version 3.0)

5 APPROVALS

Sign	Date
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