SOP number	**52.015**	Version	**2.0**
Title	**Phase I First in Human Committee Review Process**		

Prepared by Signature	Emma Whitelaw Date
Approved by Signature	Caroline Watson Date
Released by Signature	Julie Brittenden Date

SOP category	NHS GG&C Hosted R&I
Staff category	

Staff Category	**R**	**A**	**C**	**I**
R&I Governance Manager		X		
Chair of Phase I First in Human (FIH) Committee	X			
R&I Director	X			
Phase I FIH Committee Reviewers	X			
Principal Investigators (PI) involved in FIH process	X			
Research Co-Ordinator (Sponsor and Commercial)	X			
R&I Research Facilitators involved in FIH process	X			
Chair of Beatson Clinical Trials Executive Committee (CTEC)	X			
R&I Research Governance Facilitator	X			
Lead Pharmacist Clinical Trials/ R&I	X			
NHS GGC Site Clinical Trial Pharmacists involved in FIH process	X			
Glasgow Clinical Research Facility (GCRF) Manager			X	

1. Scope

This procedure applies to

- R&I Research Coordinators and R&I Research Facilitators when receiving notification of new Phase I FIH trials to ensure process is followed prior to granting R&I approval for the trials.
- Chair of Phase I FIH Committee, Phase I Committee Reviewers, Chair of CTEC and R&I Director in confirming risk categorisation,
- the PI in submitting a risk assessment form,
- the NHSGGC Site Clinical Trials Pharmacist in assisting the completion of a risk assessment form
- Research Governance in processing any recommendations, and
- The Phase I FIH Committee in reviewing a Phase I FIH or high risk clinical trial hosted within NHS Greater Glasgow and Clyde Health Board.

2. Purpose

This procedure covers the local process in assigning risk, submitting and reviewing a Phase I FIH clinical trial of investigational medicinal product (CTIMP). The purpose is to ensure that patient safety is of the highest priority during the conduct of these clinical trials and ensure that safeguards are in place to mitigate any risks that have been identified during the review process.

3. Procedures

The process detailed in Figure 1 (Phase I FIH Committee Review Process) describes the

- Role of the PI in assigning the risk category to the IMP and hence the trial.
- Role of the R&I Research Co-Ordinator or R&I Research Facilitator in providing the required documentation and information to the PI, Research Governance and subsequently the Phase I FIH committee to ensure appropriate local approvals are in place prior to granting R&I approval for the clinical trial.

3.1. Assigning a Risk Category

The PI will complete Form 52.015A - Risk Categorisation of the IMP(s), to assign the risk category. If assistance is required to complete any relevant sections in Form 52.015A, the PI should contact the Site Clinical Trials Pharmacist and/or Lead Pharmacist Clinical Trials/R&I. This form will be sent to the R&I Co-Ordinator who will submit to the Research Governance facilitator and/or chair.

Risk Categories:

1 No real risk from a safety perspective – all drugs are 'standard of care' in another setting.
2 No element of first time in human and known toxicity.
3 First time in human, but low risk of unexpected toxicity or no element of first in human but unknown toxicity.
4 First time in human and unknown risk of toxicity**.**

For trials that come under the remit of the CTEC committee, the Chair of CTEC will confirm the risk rating during the CTEC review process. For non-cancer trials the chair of the Phase I committee or R&I Director will confirm the risk rating. This risk rating will be captured by e-mail and retained by the Governance Facilitator. This will be retained on a log held within the Governance Phase I folder. Trials that are considered FIH (risk category 3 & 4) by the detail in the protocol and IB and as submitted to the regulators must be reviewed by the Committee.

Trials that fall into risk category 3 with a novel combination, where the risk is deemed as 'low' or where the drug has been administered safely at another site may be discussed with the chair or deputy of the phase I committee to determine whether re-categorised to risk category 2 is appropriate. In such cases there would be no requirement to complete and submit Form 52.015B (Phase I FIH risk assessment) to the Phase I FIH committee for review.

3.2. Timescale for Reviews

The review period, covering the gathering of feedback from reviewers and the return of comments from the chair is covered as one grouped timescale. Ideally this will occur within 10 working days and this is the routine target for the process, however, in circumstances where workload and leave makes this an unmanageable target a maximum period of 21 working days is allowable at the discretion of the Chair. The Research Governance Facilitator will agree this timescale with the Chair before contacting reviewers and inform them of this.

3.3. Process for R&I Research Co-Ordinators and R&I Research Facilitators

The R&I Research Co-Ordinator or R&I Research Facilitator will ensure that the risk categorisation from Form 52.015A is recorded on SReDA for reporting purposes and will save the completed Form 52.015A - Risk categorisation of the IMP(s) within the trial e-folder (R&D subfolder).

3.3.1. If the trial is risk category 3 or 4, the R&I Research Co-Ordinator or R&I Research Facilitator will provide Form 52.015B - Phase I FIH risk assessment to the PI for completion and return to the R&I Research Co-Ordinator to submit to the Phase I FIH Committee for review.

3.3.2. If the trial is risk category 3 or 4, the R&I Research Co-Ordinator or R&I Research Facilitator will notify the local investigator to contact:

- NHSGGC Site Clinical Trials Pharmacist to
  - ensure the Pharmacy site delivering the service is aware that a FIH trial (or high risk) is planned and that resource is available
  - Assist the PI in the completion of the relevant sections of Form 52.015B - Phase I FIH risk assessment.
- The GCRF Manager (when the trial is supported through the GCRF) to ensure the GCRF site delivering the service is aware that a FIH trial (or high risk) is planned and that resource is available.
- The R&I Research Co-Ordinator or R&I Research Facilitator will send the following documents to the R&I Governance Facilitator to initiate the Phase I FIH Committee review process:
  - A completed Form 52.015A - Risk categorisation of the IMP(s),
  - A completed Form 52.015B - Phase I FIH risk assessment,
  - MHRA and REC approvals (with comments if available),
    - It is the responsibility of the R&I Research Co-Ordinator to ensure the MHRA and REC approvals match the version of the protocol submitted.
  - the approved protocol and investigator brochure(s)
  - CVs of the health professional administering the IMP (unless already submitted within the previous two years).

3.3.3. The R&I Research Co-Ordinator will incorporate any conditions and recommendations provided by the Phase I FIH committee into the NHSGGC Board R&I Approval Letter (SOP 52.001).

3.4. Process for R&I Governance Team, Chair of Phase I FIH Committee and Phase I FIH Committee Reviewers

3.4.1. The terms of reference for the Phase I FIH committee are approved and periodically reviewed by the Glasgow Health Science Partnership Regulatory Affairs Group (GHSP RAG). The Phase I FIH Committee will review trials risk categorised 3 or 4.

The R&I Governance Facilitator will email the information received from R&I Research Co-Ordinator, detailed in 3.3.2, to the Chair of the Committee and request a list of reviewers from the core committee. In order to accommodate absences the R&I Governance Manager/ facilitator will select the reviewers on behalf of the Chair or deputy chair, if the Chair or deputy chair is on leave or who has not responded after two attempts at contacting and after 5 working days has passed.

If incomplete documents are received –these will be requested by the R&I Governance Facilitator. The clock will only start if a complete and accurate document set are received. On occasion additional information may be requested which may impact review times – PIs will be kept informed by the Governance Facilitator.

3.4.2. A minimum of 4 core members will be contacted and provided with all submitted documentation by the R&I Governance Facilitator.

3.4.3. The selected reviewers will review the documentation, complete Form 52.015C (Phase I FIH) and return to the R&I Governance Facilitator within the agreed timescale, non-adherence to this timeline is covered in 3.4.7.

3.4.4. The R&I Governance Facilitator will compile and submit the reviewers' comments to the Chair in Form 52.015D (Phase I FIH review).

3.4.5. The Chair (or deputy) of the Phase I FIH Committee will provide comments to the R&I Governance Facilitator who will notify the Reviewers, PI and the R&I Research Coordinator via email within the timeframe described in section 3.2.

3.4.6. The Phase I FIH committee will also review any significant changes to the trial that may occur prior to first global dosing, but after initial Committee review when submitted by the PI. For example, a substantial amendment which impacts on the risk/benefit of the trial.

3.4.7. If timelines are not adhered to by reviewers it is expected that they notify the R&I Governance Facilitator at the time of the initial request to review to allow the R&I Research Facilitator and Local Principal Investigator to be updated of the delay. The R&I Governance Facilitator will contact the Chair or Deputy of the committee to update. If the 21 working day deadline is not met the R&I Governance Facilitator will notify the chair who will make the decision to approve the study or request an extension to the timescale. In the absence of the Chair or Deputy, the R&I Governance Manager will follow up on their behalf.

3.4.8. If the trial is FIH for global dosing at an NHSGGC site the trial will be audited during the course of the trial to ensure recommendations by the committee have been adhered to.

3.5. Process for Principal Investigators

3.5.1. The PI will provide the R&I Research Coordinator or R&I Research Facilitator responsible for the overall approval of the trial with the following:

- After identification of a category 3 or 4 through submission of Form 52.015A the PI will send Form 52.015B (Phase I FIH risk assessment) (following discussion with Pharmacy and when applicable CTEC or GCRF manager),
- The approved protocol and Investigator Brochure(s)
- MHRA and REC comments if available,
- PI CV and CVs of any other health professional administering the IMP (unless already submitted within the previous two years).

3.5.2. The PI will make all efforts to comply with the conditions and recommendations from the Phase I FIH Committee.

3.5.3. The PI will give access to the R&I Governance Manager to allow a check of the trial to be conducted to ensure the Phase I FIH committee conditions and recommendations have been met.

3.5.4. The PI will notify R&I of any substantial amendments that impact on the risk /benefit of the trial to allow the Phase I FIH committee to review any significant changes to the trial prior to first global dosing that may alter the risk assessment.

3.5.5. The PI will notify R&I Governance of any global SUSARS or urgent safety measures that arise during the trial, after the Sponsor has notified the PI.

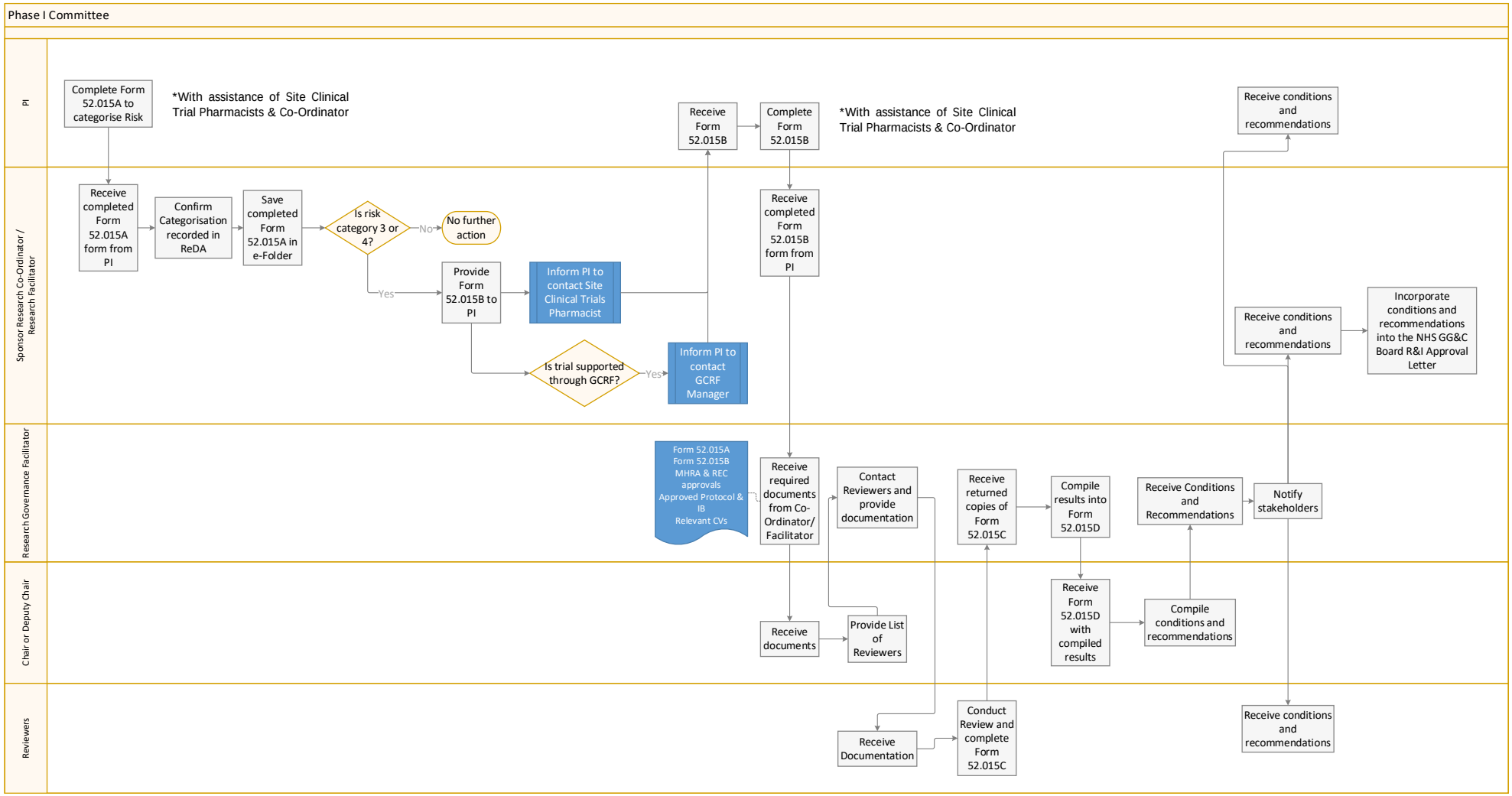

Figure 1: Flow diagram of processes involved in NHSGGC Phase I Committee Review of First in Human Studies

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3.6. FIH Trials with GMO Products

Clinical trials with GMO products require to be risk assessed to meet legislative requirements. In order to reduce the number of risk assessments for PIs to complete for these trials, once the GM Safety Committee has approved the GM Risk assessment this may be submitted to the Chair of the Phase I Committee for review along with the Risk Categorisation of the IMP(s) Form 52.015A. The Chair of the Phase I Committee will advise if Phase I Risk Assessment (Form 52.015B) is required in addition to the risk assessment already undertaken or if the risk assessment undertaken via the GM Safety Committee and Form 52.015A is sufficient.

3.7. Phase I FIH minutes/reports

An annual meeting of all Phase I FIH committee members will occur and the following will be presented:

- Number of Phase I trials submitted, and number in each risk category 1 – 4 (held by Chair and R&I Governance facilitator)
- Number of patients recruited to Phase I trials, and number in each risk category 1 – 4
- Any safety issues
- Any major issues raised during audit.

Minutes shall be recorded by the R&I Governance Facilitator, and will also be submitted to GHSPRAG and Board Clinical Governance Forum.

4. Referenced documents

- Form 52.015A - Risk Categorisation of the IMP(s)
- Form 52.015B - Phase I FIH Risk Assessment
- Form 52.015C - Reviewer's Comments
- Form 52.015D - Combined Reviewers' Comments
- SOP 52.001 - Obtaining NHS Management Approval Non-Commercial

5. Related documents

- None

6. Document History

Version	Date	Description
1.0	14/08/2019	First Release
2.0	20/12/2023	Timescale for review, change of author, process to be followed if there are delays in timescale