

SOP 17a Associated Document 1

MHRA regulated and good practice for non MHRA regulated Sponsored modifications guidance for the JRMO

Sponsored modifications Guide specifically for the MHRA regulated studies but also good practice for non MHRA regulated studies

Queen Mary University of London or Barts Health NHS Trust is sponsor for the study.

1. Research Governance Specialist (RGS) or delegate, review of sponsored modifications

RGS review should include, but is not limited to:

- Is the application valid (this includes the following as a minimum; completed modification tool, confirmation of cost form, Modification log, cover letter if substantial, clean and tracked versions of all relevant documents)
- Administrator create EDGE modification workflow on sponsor green level (this should be done as you work through the modification as per EDGE manual)
- Save all documents and correspondence into study folder under CI's name (name folder after amendment number and date e.g. SM1, MOID 1, Minor Modification 11)
- Ensure the number of the modification is correct by checking historical modifications.
- The RGS /RMGO must verify that all prior minor modifications that have not already been notified to regs via a previous substantial modification are listed in the cover letter accompanying the next new Substantial modification submission. This can be done by checking cover letter against the modification log. Any missing references should be queried before review proceeds.
- Check previous modifications and workflows have been completed.
- Review modification and ensure the modification tool has generated the appropriate classification (substantial (if so, route A or B, and if route B whether it is category A, B, or C), modification of an important detail, or minor modification). Examples of modification types here <https://www.hra.nhs.uk/planning-and-improving-research/policies-standards-legislation/clinical-trials-investigational-medicinal-products-ctimps/clinical-trial-regulations-reform/guidance-on-changes-to-the-clinical-trials-regulations/definitions-and-terminology/update-to-amendment-terminology/>
- Change section of tool: each change should be listed separately in tool, ensure each change has explanation & justification and assess if any changes need any documents updated (protocol, PIS, ICF etc)
- Ensure consistency between documents and versions are updated correctly
- If change is regarding the number of patients, ensure statistical section is updated within the protocol.
- Does the change require existing patients to be reconsented?
- Is there a change of primary and secondary objectives/end point – if it is a total change, advise this should be a new study submission.
- Do any changes have a cost implication? (Assess impact of cost for each change). If the cost form has implications, forward to costings team. If the form states no cost but they are increasing recruitment target, adding additional samples/tests etc, check with costings to see if they have the budget for this.
- Is cost form accurate? (ie extension is never no cost)
- Is there a new vendor? (Let preaward team know)
- Does change move away for protocol mandated text or our SOPs?
- If the change is of CI/local Investigator - CV and GCP provided (and checked) and new sponsor-CI agreement signed if change in CI.

- Does the modification require approval from any other stakeholders? E.g., support department, GCP manager
- Is change a result of audit or non-compliance? if so, check with auditor or QA manager (respectively)
- If the modification is a substantial change seek confirmation TSC aware and agrees (email or minutes)
- Once modification is finalised and support department/GCP approval (if required) has been obtained, sign the modification tool off as: Dr Mays Jawad, research.amendments@qmul.ac.uk. The modification date will be the date you lock the tool and this date should be entered into the modification log and then sent back to research team/CI together with the locked PDF version of the modification tool.
- For minor modifications, issue email template appendix E with the locked tool attached. This is also approval to implement the modification.
- For all other modifications, issue email template appendix B with the locked tool attached. This approval permits submission of the modification but not to implement the modification.
- Once REC/MHRA CAG and HRA approvals (whichever are applicable) have been issued, cross-check the documents to ensure we have the final documents as listed in the REC approval letter (if REC approval is issued)
- Finally issue final sponsor confirmation to implement the modification using template email appendix C/D depending on modification type

1.1. MHRA regulated minor modifications needing GCP Manager review:

The GCP managers do not need to review minor modifications to the study but should be informed of every modification and issue the usual GCP manager approval to RGS/RMGO.. If you are unsure – please ask your GCP manager.

2. GCP managers review

GCP managers review is additional to the RGS/RMGO review (like the support departments) and should cover (as a minimum):

- GCP and regulatory compliance
- Monitoring changes
- IMP change (pharmacy) including RSI
- Risk assessment update, if required
- Change of sponsor CI or statistician – are they suitable (assess CV and GCP)
- Increase in site number – can monitoring be covered?
- New vendor assessment
- Advise team to update CRF if applicable
- Advise team to update any contracts if applicable

3. Halted

SOP Point 11 described process when a study is 'halted'.

A temporary halt is defined as a stoppage of either the trial or one or more research sites not foreseen in the protocol, but with the intent to resume the trial in the future

For CI/local Investigators on long term leave (3+ months), a modification to temporarily replace the CI/Investigator should be submitted.

4. Submission of documents to MHRA

Studies submitted to REC and MHRA via Combined review IRAS should submit modifications via CR IRAS portal, however those set up prior to the introduction of CR should submit via the MHRA Submission Portal. Further guidance can be found at <https://www.myresearchproject.org.uk/help/hlpamendments.aspx#Amendment-Tool>