Standard Operating Procedure			**51.014**
Preparation and submission of IRAS forms			
Version	4.0		
Prepared by	Maureen Travers	Signature	Date
Approved by	Melissa Robert	Signature	Date
Released by	Julie Brittenden	Signature	Date

1. SOP Category
NHS GG&C Sponsor R&I

2. Staff Category
Research Co-ordinators (Sponsor Representatives)
Research Facilitators
Sponsor Pharmacist
Innovation Contracts Manager (Innovation Co-ordinator; Sponsor Representative)
Innovation Project Manager
University of Glasgow Research Governance Manager & Officer
Chief Investigator

3. Scope
This procedure applies to NHS Greater Glasgow and Clyde staff with responsibility for review of IRAS submissions to Research Ethics Committees, R&I Departments, and Regulatory authorities (e.g. Medicines and Health Regulatory Authority (MHRA))within the Glasgow Clinical Trials Unit (CTU).

4. Purpose
To describe NHS GG&C process to review and approve Integrated Research Application System (IRAS) forms when NHS GG&C is the study Sponsor/Co-Sponsor.

The IRAS system covers applications to multiple regulatory agencies; however, this SOP specifically details submissions to a Research Ethics Committee, R&I and the Medicines and Healthcare products Regulatory Agency (MHRA). It is noted that this activity is primarily performed by staff with Sponsor responsibilities. R&I management review and approval is a separate process (However, it may be delivered by the same staff member).

5. Procedures
5.1 Submission of Applications
The risk associated with any project should be assessed prior to review and approval of IRAS application submissions.

Applications to the MHRA, Ethics and R&I can be done in parallel but this is not a requirement. Completion of applications to all three organisations (and others) is done through the IRAS online system – https://www.myresearchproject.org.uk
Anyone is able to sign up for an IRAS account and there is a training module and help sections on the website. All IRAS accounts must have an email address and be password protected.

Example forms are also available on the IRAS website for guidance.

- For Clinical Trials of Investigational Medicinal Products (CTIMPs), applications must be made to the MHRA, Ethics and R&I.

- For Clinical Investigations of non-CA marked Medical Devices, applications (CIA) must be made to the MHRA, Ethics and R&I.

- For Research studies (Non-CTIMPs; device studies that are not Clinical Investigations), applications must be made to Ethics and R&I.

- For studies involving only staff (as participants), the application is made to R&I only.

- For tissue banks, databases, registries etc, application is made to Ethics only. Documents listed in the Ethics favourable opinion letter should be submitted to and acknowledged by R&I before the study can proceed.

General and question-specific guidance can be found on the IRAS website – https://www.myresearchproject.org.uk/Help/UsingIRAS.aspx

5.2 Personnel responsible for completion of IRAS forms, approval and submission

The forms will be completed by the Chief Investigator (CI) or by a delegated individual (e.g. Project Manager, Research Assistant, R&I Pharmacists, etc.). The person completing the form needs to have an in-depth knowledge of the trial in order to be able to complete the appropriate sections with the correct information. In addition, this person needs to have an understanding of the electronic IRAS system and be familiar with the layout of the specific web pages and the options to transfer the forms for review and ultimately for authorization by the Sponsor organization.

Where specific sections require experts to complete the information (e.g. Part B) then the relevant person/people will be consulted. For example, Part B Section 1 requires R&I pharmacist review and Section 3 should be completed by appropriate personnel from Medical Physics and Clinical Radiology. Furthermore, for all CTIMPs, there are also other accompanying documents that need to be prepared as part of the CTA submission e.g. sIMPD, SmPC, labels. Sponsor Pharmacy will always be involved in their review.

For proof of concept feasibility studies of non-CA marked medical devices that are at too early a stage to go to the MHRA, safety sign off is required in Part B Section 2 from Head of Clinical Engineering or equivalent. For all Clinical Investigations of non-CA marked medical devices, there are also other accompanying documents that need to be prepared by the Manufacturer as part of the CIA e.g. device details, instructions for use, labels, summary of bench & pre-clinical testing, Clinical experience to date, manufacturer's standards. The innovation sponsor team will always be involved in the review of these documents.

As the representative of the Sponsor or Co-Sponsor of a study, it is the responsibility of the R&I Co-ordinator to ensure all the appropriate experts have been consulted for the preparation of the applications. The R&I Co-ordinator must then review and sign the applications on behalf of the Sponsor, providing authorisation. This includes the R&I, Ethics and the CTA or CIA for the MHRA, when appropriate. Alternatively, submission of the IRAS forms can be delegated to the CI, in which case a full copy of the submission documents should be sent to the Research Co-ordinator. If the CI is delegated to complete the submission, the R&I Co-ordinator must approve the submission on behalf of the Sponsor following the appropriate checks (SOP 51.018). For CTIMPs, these checks should be documented in the Sponsor checklist, which is completed by the R&I Co-ordinator.

5.2.1. Clinical trial application to MHRA

Not all studies that involve drugs are considered to be CTIMPs. This should be discussed with the R&I Co-ordinator and Sponsor Pharmacist. In some cases, applications may need expert pharmacy advice. In addition, the MHRA website should be consulted for clarity –Medicines and Healthcare products RegulatoryAgency-gov.uk

A Notification Scheme is now available for lower risk CTIMPs – http://www.mhra.gov.uk/Howweregulate/Medicines/Medicinesregulatorynews/CON114358. It is the Sponsor's responsibility to determine the level of risk of each CTIMP study. The R&I Co-ordinator, on behalf of the Sponsor, should consult with Sponsor Pharmacy to determine the level of risk.

The CI can be delegated the task of submitting the CTA or CIA to the MHRA on behalf of the Sponsor/Co-Sponsor. In this case a letter authorising this should be provided by the R&I Co-ordinator on behalf of the Sponsor. Before issuing the letter, the co-ordinator should perform a check to ensure that final versions of study documents (e.g. final protocol) are available. The R&I Co-ordinator will still retain oversight of the CTA or CIA application and document review, submission and authorisation dates in the Sponsor oversight checklist.

Depending on the study phase, the MHRA charges different application fees. Up-to-date details on these can be found on the MHRA website.

5.2.2. Ethics application

Detailed information on ethics applications can be found on the Health Research Association Service (HRA) website – http://www.hra.nhs.uk/research-community/applying-for-approvals/

NRES now has a Proportionate review procedure for low risk studies – http://www.nres.nhs.uk/applications/proportionate-review/

The application is the same as for full-review studies; however, the review process is proportionate to the reduced risk of the project and the response time is within 14 rather than 60 days.

Checklists are available to ensure that all of the correct documentation is submitted to the different organisations – see MHRA and HRA websites.

5.3 Review

Forms can either be transferred electronically through IRAS to the R&I Co-ordinator using their IRAS ID (email address) or the Researcher can save a pdf of the draft form and email that to the R&I Co-ordinator.

Review of the IRAS form should include; a) ensuring that the project filter questions have been correctly selected b) that the study details on the form match the protocol or clinical investigation plan (CIP) and c) that the procedures, people and other information listed are accurate and appropriate.

It is particularly important that the filter questions are answered correctly as these will determine which forms and questions are generated by the IRAS system.

5.4 IRAS form authorisation

The IRAS forms can be signed (electronically) by the relevant individual through the electronic authorisation system. For CTIMPs or Clinical Investigations of non-CA marked medical devices, the R&I Co-ordinator will note on the Sponsor checklist when the application was signed.

Authorisation of the IRAS forms by the R&I Coordinator indicates that the study has been reviewed and approved, for submission, on behalf of the Sponsor.

5.5 Submission

5.5.1 MHRA

Submission to the MHRA should be electronically using the CESP system (https://cespportal.hma.eu/Account/Login?ReturnUrl=%2f)
Details on what should be sent can be found here:
http://www.mhra.gov.uk/Howweregulate/Medicines/Licensingofmedicines/Clinicaltrials/ApplyingforaclinicaltrialauthorisationWhattosend/index.htm

If submission is done by the CI or Manufacturer on behalf of the Sponsor then a full copy of the submission documents should be sent to the R&I Co-ordinator.

5.5.2 Ethics

Ethics should be contacted prior to submission in order to book a meeting through the Central Allocation System
(CAS – http://www.nres.nhs.uk/applications/booking-and-submitting-your-application/central-allocation-system/.

Note that it is important to have the study reviewed by the correct committee type (CTIMP, study involving Adults with incapacity), this can be discussed with local Ethics contacts but will be confirmed by CAS at the time of submission.

If the submission is delegated to the CI on behalf of the Sponsor then a full copy of the submission documents should be sent to the R&I Co-ordinator for the appropriate folder.

5.5.3 R&I

Submission to R&I is electronic (currently via Email or via NRS permission CC). If the study is multi-centre then R&I submission should also go through NHS Research Scotland Permissions Coordinating Centre (www.nrspcc.org); this is usually done by the CI or their designee.

Submission to R&I should include all of the local documents (e.g. Organisational Information Document (OID). Collectively the local document submission is referred to as a Local Information Pack (LIP). This pack contains local details of the study and is completed outwith the IRAS electronic system (currently).

5.6 Response

Approvals from each of the IRAS submissions will be held in the study Sponsor file.

5.7 Voluntary Harmonisation Procedure (VHP)

In situations where NHS GG&C have been requested to undertake the role of UK lead co-ordinating centre for a CTIMP, submissions to Ethics, R&I and the MHRA are made via IRAS. Ethics and R&I submissions should be prepared and submitted as described above.

The lead Sponsor may submit to their local competent authority via the Voluntary Harmonisation Procedure – http://www.hma.eu/fileadmin/dateien/Human_Medicines/01-About_HMA/Working_Groups/CTFG/2010_03_VHP_Guidance_v2.pdf. In this case, once the lead Sponsor has received a 'positive decision' from their competent authority under VHP, each participating country should be notified to proceed to the National Step formal CTA.

In the UK, submission to the MHRA must be received within 21 days. The submission documents must be those that were reviewed under the VHP assessment, the VHP positive decision letter plus any documents specifically required by the MHRA. The EudraCT xml must be imported to IRAS.

The labels to be used in the UK should be reviewed by Pharmacy to ensure compliance with UK legislation.

All correspondence with the MHRA must contain the VHP reference number as well as the EudraCT number. The MHRA will respond within 10 days of receipt of the submission. The standard fees still apply.

6. Referenced documents

N/A

7. Related documents

SOP 51.007 Identifying a Sponsor organization
SOP 51.018 Sponsor Oversight Checklist
IRAS Website- https://www.myresearchproject.org.uk
MHRA Website - http://www.mhra.gov.uk
NRES Website - http://www.nres.nhs.uk
NRSPCC - www.nrspcc.org
HMA Website - http://www.hma.eu

8. Document History

Version	Date	Description
1.0	05/02/2013	Release of first version
2.0	14/07/2016	Updated to template v1.4, SOP renumbered and clarification of content
3.0	12/03/2020	Author amended Staff category updated Process and procedures updated Local submission information updated SOP version updated "Released by" updated
4.0	11/02/2022	Updated to include innovation team, clinical investigations of non-CE marked medical devices and to change R&D to R&I

This SOP is a controlled document. The current version can be viewed on the Unit's internet site. Any copy reproduced from the internet site may not, at time of reading, be the current version.