

STU-SOP-TS-009 – Standard Operating Procedure on Applying for Ethics and Regulatory Approval

Version No:	5	Effective Date:	27-Mar-2026
Description of changes:	<p>SOP reviewed in light of clinical trial regulations 2025 and GCP updates. Specific references to QPulse as the QMS have been removed. We now only refer to a QMS system.</p> <p>Updated to add in submitting for MHRA approval which was previously in its own SOP.</p> <p>Removal of APR requirements</p>		

List of Abbreviations	
APR	Annual Progress Reports
CAG	Confidentiality Advisory Group
CI	Chief Investigator
CTA	Clinical Trial Authorisation
CWOW	Combined Ways of Working
HCRW	Health and Care Research Wales
HRA	Health Research Authority
IRAS	Integrated Research Application System
NRES	National Research Ethics Service
PI	Principal Investigator
PRS	Proportionate Review Service
REC	Research Ethics Committee
SOP	Standard Operating Procedure
STU	Swansea Trials Unit
SU	Swansea University
TM	Trial Manager
TMF	Trial/Project Master File

1. Purpose

This Standard Operating Procedure (SOP) describes the procedure of applying for NHS National Research Ethics Service (NRES) Research Ethics Committee (REC) approval to conduct a research project. It also covers the procedure of applying for Medicines and Healthcare products Regulatory Agency (MHRA) approval for Clinical Trials of Investigational Medicinal Products (CTIMPs).

All trials or other research studies which involve NHS participants, time, or resources must seek approval from an appropriate NRES REC.

The information within this standard operating procedure (SOP) is summarised. Detailed guidance is available via the Health Research Authority (HRA) website: <http://www.hra.nhs.uk/research-community/applying-for-approvals/>. The process to follow for ethics approval for CTIMPs is also detailed on the HRA website.

Health related research studies which involve humans, their tissue or data but do not require NRES REC approval still require approval by an appropriate REC. In these instances, it will likely be one of the Swansea University (SU) internal RECs. The policy and guidance for submission for SU REC review can be found on the University intranet.

For international projects, there may be the requirement for a local research review, which will be additional to a UK review.

2. Background

RECs exist to protect the rights, safety, dignity and well-being of research participants whilst facilitating ethical research that is of potential benefit to participants, science and society.

The UK policy framework for health and social care (2017) requires that research involving humans, their tissue or data in the NHS must receive an appropriate ethical review. This is required for each project based on its protocol. Sub studies to the main research project with separate protocols also require an appropriate ethical review.

The HRA website details what types of projects an NRES REC can review.

The NHS REC approval system also covers other approvals and permissions e.g. health and social/community care research, prison and probation services research.

Similar local regulations and requirements are in place in other countries across the world.

For CTIMPs, a Clinical Trial Authorisation (CTA) is needed from the MHRA for the trial to proceed. The process of applying for a CTA is done in parallel with the NRES REC application on the Combined Ways of Working (CWOW) system supported by the Integrated Research Applications System (IRAS).

3. Roles and Responsibilities

The **Sponsor** has overall responsibility for ensuring that appropriate approvals are in place before research involving the NHS can begin. Although the Sponsor can delegate responsibilities for submission to any ethics committee, they remain accountable for project management and must have oversight of all delegated functions.

The **Chief Investigator** (CI) is responsible for ensuring they have identified and agreed a Sponsor prior to submitting a research project for NRES ethical review. The CI must also ensure favourable ethical opinion, local NHS R&D permission and all other relevant approvals are in place, before recruitment begins and during the study. Responsibilities may be delegated.

The **Principal Investigator** (PI) at each trial location is responsible for ensuring that ethical approval is in place or imminent prior to coordinating the local NHS R&D permission process for site approvals.

The **Trial Manager** (TM) is usually delegated the responsibility for compiling documentation for ethical approval, entering information onto the online system and coordinating signatures with the Sponsor to enable submission. The TM will also file all submission and approval documentation in the Trial Master File (TMF) and disseminate information to enable local approval processes to begin.

External use of SOP: This SOP and Associated Documents (AD) may be used for research projects not adopted by STU where Swansea University (SU) staff and associated NHS organisations require guidance. In such instances, oversight responsibility for any associated tasks will not be the responsibility of STU.

4. Procedure

The HRA website details the tasks involved in applying for ethical approval <https://www.hra.nhs.uk/approvals-amendments/what-approvals-do-i-need/research-ethics-committee-review/applying-research-ethics-committee/>

4.1 Agreeing the Research Sponsor

Sponsor arrangements for the research project must be confirmed before a project can be submitted for NRES ethical review, as a signature on behalf of the Sponsor is required. It is usual for the substantive employer of the CI to be the Sponsor or, for student projects, the registered University.

For all research projects please follow the Sponsor's review processes prior to preparing a submission for ethics (and MHRA) approval. This may involve completing a Sponsor assessment. Only once sponsor approval has been given should the submission for ethics (and MHRA) approval progress. The sponsor should issue a **sponsorship letter** to be submitted as part of the application pack.

4.2a Completing the application form on the IRAS system

Applications for research studies that are not CTIMPs must be made on the standard form available from IRAS at www.myresearchproject.org.uk.

For help and guidance on creating an account or using IRAS please consult <https://www.myresearchproject.org.uk/help/hlpethicalreview.aspx>.

When the project application form is complete (the full data set), it should be electronically authorised by the CI, other relevant signatories and Sponsor. Any change made must be approved by the Sponsor.

Any access or change made to the IRAS form after electronic signatures have been assigned will invalidate all signatures.

The online system will automatically generate an 'Applicant's Checklist' for completion (one for the ethics application and any other review bodies required). Completion of the checklists are required for a valid submission to the REC with the IRAS form and all supporting project documents outlined.

4.2b Preparing an IRAS form and documents for submission to the REC

Step by step instructions can be found on the 'E-submission' tab within the IRAS system. Each step of this process must be followed or the application to the REC will not be valid. There is also a verification tool available to help assess if all required documents and steps are passed.

The REC will send an email with an attached letter indicating whether the project is valid or not. The letter will also invite the CI, key investigators and the Sponsor to attend the virtual REC meeting, at a specific time.

4.2c Completing the application form on the CWOW system

Applications for research studies that are CTIMPs must be made on the CWOW system managed by IRAS. The person responsible for creating and/or managing the online application will need to sign up for an account for this system separately to an IRAS account.

The CWOW system allows the parallel submission of trial documents for REC and MHRA review. The MHRA website outlines the process to be followed <https://www.gov.uk/guidance/clinical-trials-for-medicines-apply-for-authorisation-in-the-uk#registration-of-your-clinical-trial>

The documents needed for CWOW are listed on the HRA website <https://www.hra.nhs.uk/planning-and-improving-research/policies-standards-legislation/clinical-trials-investigational-medicinal-products-ctimps/combined-review/document-management-combined-review-applications/>.

4.3 Submitting the project application

When all project documents are finalised and the required signatures have been obtained, the project application must be booked into a REC through the Online Booking Service and submitted to the allocated REC (or your selected REC) electronically through IRAS/CWOW on the same day that you book for ethical review.

Online Booking Service

The online booking service is used for all IRAS form applications for project-based research in the NHS (or HSC in Northern Ireland) view and for HRA approval where required.

When booking, you will require access to your application form as questions will be asked to determine which RECs are suitable, depending on study type. Some project applications must be reviewed by a flagged REC, e.g. CTIMP RECs. Some projects may be suitable for the proportionate review service (PRS). You will be asked to respond to questions for the system to determine this.

On the day of booking an email confirmation will be received containing the REC name and project reference.

Proportionate Review Service

If the project is suitable for PRS, this will be highlighted as an option by the online booking service.

PRS provides an accelerated, proportionate review for research projects which raise no material ethical issues, have minimal risk, burden or intrusion for research participants. These applications are reviewed by a Sub-Committee of a REC. The review is as rigorous as a full REC review and will not affect the opinion given. The final decision of the review is notified to the applicant by email with a letter attachment.

4.3 Validating the project application

Applications will be validated by the REC (and MHRA for CTIMPs) to confirm validity i.e. all mandatory documents are present and in the correct file format. This should be done within 1 working day. Issues must be addressed within 7 working days or else the submission will be invalidated. The timelines and process for review can be found at <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/the-approvals-process-for-clinical-trials/the-approvals-process-for-applications/>

4.4 Reviewing the project application

An initial review will be done by the REC (and MHRA for CTIMPs) in parallel and the outcome will be shared with sponsor within 30 days of the validation.

There are three possible outcomes from a REC review:

- 1) Favourable.
- 2) Favourable subject to conditions.
- 3) Unable to issue a favourable decision and request further information.

For a CTIMP, the MHRA will either issue a CTA or may have further queries. **The trial cannot progress until the CTA has been issued by the MHRA.** Information about CTIMPs on the HRA website can be found at <https://www.hra.nhs.uk/approvals-amendments/what-approvals-do-i-need/research-ethics-committee-review/applying-research-ethics-committee/ctimps-sl-ar1/>

The REC opinion (and the MHRA decision for CTIMPs) will form the outcome of the initial review. If the REC and/or the MHRA are unable to approve the trial at this stage, a request for further information will be consolidated and issued.

If sponsors need longer than 60 days to respond, they can ask for an extension. Sponsors can do this by contacting the REC directly or, for MHRA-related queries, at clintrialhelpline@mhra.gov.uk.

4.5 Health Research Authority (HRA) and Health and Care Research Wales (HCRW) Approval

Research teams should always check the HRA or HCRW websites to ensure the most up to date process is followed. An overview of the current process is below.

The HRA and HCRW Approval brings together the assessment of governance and legal compliance with the independent ethical opinion provided by a REC (and MHRA opinion for CTIMPs) for the NHS in England and Wales and is required for all project-based research involving the NHS and Health and Social Care. This replaces the need for local checks of legal compliance at each participating organisation in England and Wales. Participating organisations now focus their resources on assessing, arranging and confirming their capacity and capability to deliver the research project.

For new studies led from Scotland or Northern Ireland with English or Welsh sites, the national R&D coordinating function of the lead nation will share information with the HRA and HCRW Approval teams who will assess and issue approval for English and Welsh sites.

For projects which have gained approval prior to the HRA and HCRW approval process, subsequent amendments for projects which have NHS sites in England will need to use the current process.

4.6 Confidentiality Advisory Group – Research or Non-Research projects

Research and non-research projects involving access to confidential patient information without consent in England and Wales should apply to the Confidentiality Advisory Group (CAG).

Research applications are prepared by completing a form on the IRAS/CWOW system. Supporting document requirements are set out in the checklist for the form.

Non-research applications should complete the section 251 form. Supporting document requirements are set out in the annexe to the form.

The HRA provides information on precedent set categories. These are common situations which have been identified and a precedent for the processing of these agreed by the CAG. Applications under a set category will be processed in a timelier manner than those outside the set categories.

All documents should be provided in black and white, labelled with a title, version number and date. Application forms should not include embedded documents.

Detailed information on the CAG, application guidance and information on completing the IRAS form or section 251 form are available from the HRA website:

<https://www.hra.nhs.uk/approvals-amendments/what-approvals-do-i-need/confidentiality-advisory-group/>

All CAG approvals are reviewed annually to assess the need for continuing approval using an annual report template located at:

<https://www.myresearchproject.org.uk/help/hlpconfidentiality580.aspx#CAG-annual-review>.

The report must be submitted 4 weeks prior to the current approval expiring.

4.7 Post-approval requirements for the trial

The REC favourable opinion letter (and CTA for CTIMPs) must be filed in the TMF alongside copies of the signed IRAS/CWOW application, the supporting documents submitted for review and any correspondence relating to the review process. If the project involves multiple sites, a copy of the favourable opinion letter (and CTA for CTIMPs) should be sent to each PI for inclusion in each trial location's site file.

The research project should start within 12 months of the date of the favourable opinion from the REC. A research project is generally considered to have commenced when any procedures in the protocol are initiated. Where research does not commence within 12 months, the CI should inform the REC in writing. An Annual Progress Report (APR) was required for studies up to 1st Aug 2024 but are no longer required.

If the project does not start within 24 months, a further explanation should be given to the REC in writing. The REC may remove the ethical opinion and decide that a new application is required, or they may grant a further 12 months of approval.

After the initial approval decision, the REC must approve all substantial modifications to the protocol.

Any changes to the end date specified in the application should be notified as a non-substantial modification.

All modifications must be approved by the Sponsor before submission. The approval of modifications to the research project is described in STU-CT039 Substantial and Non-substantial Modifications.

It is a condition of the REC favourable opinion that **all clinical trials are registered** in a public registry before the first participant is recruited and no later than six weeks after (<https://www.hra.nhs.uk/planning-and-improving-research/research-planning/research-registration-research-project-identifiers/>).

Registries include ISRCTN (<https://www.isrctn.com/>) and Clinicaltrials.gov (<https://clinicaltrials.gov/>). Applications using CWOW automatically add your project to ISRCTN, but other studies may need to be manually added by the CI or TM. Registries for non-clinical trials are available.

5. References

- Health Research Authority website (HRA) - <http://www.hra.nhs.uk/>
- UK policy framework for health and social care research (2017) - <https://www.hra.nhs.uk/planning-and-improving-research/policies-standards-legislation/uk-policy-framework-health-social-care-research/>
- Swansea University online research ethics application system - <https://www.swansea.ac.uk/research/research-integrity-ethics-governance/research-ethics/new-online-research-ethics-system/>
- HRA approvals process for clinical trials (updated Oct 2025) <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/the-approvals-process-for-clinical-trials/>
- HRA – CTIMP Standard Conditions webpage (updated Jul 2024) <https://www.hra.nhs.uk/approvals-amendments/what-approvals-do-i-need/research-ethics-committee-review/applying-research-ethics-committee/ctimps-sl-ar1/>

6. Associated Documents

Number	Title	Location
N/A	N/A	N/A