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| **GD\_001 GUIDANCE DOCUMENT:** **GAINING AND MAINTAINING RESEARCH AUTHORISATIONS INCLUDING HRA AND MHRA** |
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| **1**. **Purpose**  Navigating the different authorisation systems for clinical research can be challenging. This document is intended to provide guidance to researchers in how to gain and maintain authorisations for research in the NHS. More detailed information about the processes mentioned in this document should be sought from the specific websites referenced in the first instance. Further assistance should be sought from the R&D department if required.   1. **Abbreviations**  |  |  | | --- | --- | | **ARSAC** | Administration of Radioactive Substances Advisory Committee | | **CI** | Chief Investigator | | **CTIMP** | Clinical Trial of an Investigational Medicinal Product | | **GCP** | Good Clinical Practice | | **HEI** | Higher Education Institute | | **HRA** | Health Research Authority | | **IRAS** | Integrated Research Application System | | **MHRA** | Medicines and Healthcare products Regulatory Agency | | **REC** | Research Ethics Committee | | **R&D** | Research & Development | | **RMO** | Research Management Office | | **SOP** | Standard Operating Procedure | | **UHBW** | University Hospitals Bristol and Weston NHS Foundation Trust |  1. **Research, Audit or Service Evaluation**   After a project has been identified, the project lead should review whether the work they wish to carry out is research. The HRA website provides information on the definition of research and the following link will support that decision making process: <http://www.hra.nhs.uk/research-community/before-you-apply/determine-whether-your-study-is-research/>. If the work is not research, and can be defined as audit or service evaluation/development the project lead must contact the Trust audit team. If the work has been identified as Service Improvement the project lead must contact the Trust Transformation team.   1. **Funding**   Any applications for funding associated with the research must be discussed with the R&D department to ensure costs are appropriately covered; please contact the Research Grants Manager and refer to the *SOP\_003 Developing and Designing your study UHBW*  for further details.   1. **Sponsorship**   Under the UK Policy Framework for Health & Social Care Research all clinical research requires a sponsor and relevant authorisations must be in place prior to the study commencing. To apply for UHBW sponsorship please refer to the SOP\_*002 Research Sponsorship at UHBW* for the application process.   1. **Authorisations required**   There are national systems for gaining authorisations and the HRA website, which describes these systems, should be used as reference for those processes. For studies delivered at UHBW, the Research Management Office (RMO) will also provide advice and guidance in navigating these, where required, and can be contacted on 0117 342 0233.  **6.1 HRA approval**  HRA Approval is the process for the NHS in England that brings together the assessment of governance and legal compliance and is undertaken by dedicated HRA staff, with the independent REC opinion provided through the UK Health Departments’ Research Ethics Service.  Consequently, all proposed research within the NHS (e.g. using patients, staff or NHS facilities) must apply for HRA approval by completing and submitting application forms and associated documents (e.g. protocol, Patient Information Sheets and Informed Consent Forms etc.) on the Integrated Research Application System (IRAS). More information on the submission process can be found on the HRA website and IRAS website.  **Please note** it is a requirement of the HRA to insert the IRAS reference number into the header/footer of all patient facing documents that are submitted for HRA review.  For all participating NHS sites in England you must complete an Organisation Information Document and Schedule of Events (or Schedule of Events Cost Attribution Template, as appropriate) for each *site type.* Templates are available to download on the HRA website and must be submitted through IRAS as part of the submission pack to the HRA. Please note these documents are continuously being improved and updated by the HRA. Always refer to the HRA website for the latest versions.  Your sponsor must review all of your documents prior to submission in IRAS. Where UHBW is the sponsor please email [R&DSponsorship@UHBW.nhs.uk](mailto:R&DSponsorship@UHBW.nhs.uk) to request authorisation of your IRAS form. When you are ready to submit, book your application through the Online Booking Service. Details of this process can be found on the HRA website.  **6.2 NHS Research Ethics Committee (REC) approval**  Some research is exempt from requiring NHS REC approval. See <http://www.hra-decisiontools.org.uk/ethics/> to determine whether you need to apply for NHS REC approval. Different types of NHS RECs review different types of research proposals, and there are full details provided on the HRA website.  Please note your research may require a different type of ethical review. These reviews are provided by the Gene Therapy Advisory Committee, the Social Care Research Ethics Committee, the Ministry of Defence Research Ethics Committee and the Higher Education Institution (HEI) Research Ethics Committees.  For detailed information about REC approval and the types of NHS RECs, please see the HRA website: <http://www.hra.nhs.uk/research-community/applying-for-approvals/research-ethics-committee>  Please note only a single submission through IRAS is required for both HRA and REC review (if required). Further information can be found on the HRA website.   * 1. **Authorisation from the Medicines and Healthcare Products Regulatory Agency** (**MHRA) For Clinical Trials of Investigational Medicinal Products (CTIMPs)**   CTIMPs require authorisation from the MHRA before they can proceed. Details about the application procedure are available on the MHRA website (<https://www.gov.uk/clinical-trials-for-medicines-apply-for-authorisation-in-the-uk>). For support and advice in preparing the application, which is done using IRAS, please liaise with the sponsor in the first instance.  The document that will be used as the reference safety information should be identified and specified in the cover letter to the MHRA.  **6.4 Other authorisations**  There may be other authorisations required prior to the start of the trial, depending on the type of research being carried out.   * For research requiring CAG (confidentiality advisory group) approval see: <http://www.hra.nhs.uk/resources/confidentiality-advisory-group/> * For research involving the administration of radiopharmaceuticals or sealed radioactive sources, the ARSAC notes for guidance should be used, found at: <https://www.gov.uk/government/publications/arsac-notes-for-guidance> * For research involving a clinical investigation of a non CE marked medical device authorisation from MHRA devices is required. More information can be found: <https://www.gov.uk/guidance/notify-mhra-about-a-clinical-investigation-for-a-medical-device>   If it is unclear which other authorisations are required consult with the sponsor in the first instance, and the UHBW R&D department for advice.  **6.5 Capacity and Capability Confirmation at participating sites**  For all participating sites in England an assessment of capacity and capability must be undertaken by the local Research & Development office (at UHBW, carried out by the R&D department) prior to the research commencing at the site. Further information on this process can be found on the HRA website: <http://www.hra.nhs.uk/resources/hra-approval-nhs-organisation-guidance/#NHS> or refer to *SOP*\_*017 Confirmation of Capacity and Capability to Deliver Research at UHBW*.  Please note sites outside England have different processes – please liaise with the local Research & Development department for further guidance on assessment requirements.   1. **After Trial commencement**   There are a number of other events which require notification/discussion with the MHRA (and REC) after trial commencement, listed below.  **7.1 Amendments**  Any changes to the protocol and associated documents (e.g. Patient Information Sheet, Informed Consent form etc.) after sponsorship must be agreed by the sponsor before submitting them for approval. In conjunction with the study team, the sponsor will determine and document whether protocol amendments are substantial or not, prior to authorisations being sought. Further information on submitting amendments for UHBW sponsored research can be found in the *SOP\_019 UHBW sponsored research amendments*. Please note the MHRA also requests payments to review amendments therefore please consider this in your costings and whether an amendment is necessary.   * 1. **Suspending your research, then restarting it**   If a CTIMP has to be suspended, the sponsor, MHRA and REC must be notified. The CI or delegated representative within the research team must contact the sponsor immediately to discuss this, and ensure the appropriate steps are taken to inform the REC/MHRA of the halt within the defined timeframes (at the latest within 15 days). Details of the process to halt/suspend and restart a trial are found here: <https://www.gov.uk/clinical-trials-for-medicines-manage-your-authorisation-report-safety-issues#suspend-or-terminate-a-trial>. Documents found on the MHRA website should be used as a guide to inform the discussion between sponsor and research team about suspending the trial. All discussions must be documented, and this can be done using *TMPL\_056 File note template,* or by following up with an email summary of the discussion.  For non CTIMP research, the REC must be notified. The CI or delegated representative within the research team must contact the sponsor immediately to discuss whether to suspend the study, and ensure the appropriate steps are taken to inform the REC of the suspension within the defined timeframes. Further details can be found on the HRA website. All discussions must be documented, and this can be done using *TMPL\_056 File note template.*   * 1. **Terminating your research**   If a CTIMP has to be terminated, the sponsor, MHRA and REC must be notified. The CI or delegated representative within the research team must contact the sponsor immediately to discuss this, and ensure the appropriate steps are taken to inform the REC/MHRA of the termination within the defined timeframes (at the latest within 15 days). For further details, see <https://www.gov.uk/clinical-trials-for-medicines-manage-your-authorisation-report-safety-issues#end-of-trial>. Documents found on the MHRA website should be used as a guide to inform the discussion between sponsor and research team about terminating the trial. All discussions must be documented, and this can be done using *TMPL\_056 File note template.*  For non CTIMP research, the REC must be notified. The CI or delegated representative within the research team must contact the sponsor immediately to discuss this, and ensure the appropriate steps are taken to inform the REC of the termination within the defined timeframes. Further details can be found on the HRA website. All discussions must be documented, and this can be done using *TMPL\_056 File note template*   * 1. **Urgent Safety Measures for a CTIMP**   If there are any safety issues which put a patient at risk during a CTIMP the MHRA must be notified immediately. Please refer to the *SOP*\_*009 Research Safety Reporting UHBW* for full details of how to process urgent safety measures. For further information, see the MHRA website: <https://www.gov.uk/clinical-trials-for-medicines-manage-your-authorisation-report-safety-issues#report-an-urgent-safety-issue>   * 1. **Development Safety Update Reporting**   Annual reports for CTIMPs must be submitted to the MHRA in relation to the investigational medicinal product(s) in use. Please see *SOP*\_*009 Research Safety Reporting* *UHBW* for details of how this must be managed for UHBW sponsored studies. Reports are usually due on the anniversaries of the date the MHRA authorisation was issued. Technical details for the submission can be found on the MHRA website: <https://www.gov.uk/clinical-trials-for-medicines-manage-your-authorisation-report-safety-issues#submit-development-safety-update-reports-dsurs>   * 1. **Annual Safety and Progress reports**   Annual safety and progress reports are required to be submitted to the ethics committee as a condition of the favourable opinion. Failure to do so can invalidate the favourable opinion. Both the progress and safety reports are due on the anniversaries of the date the REC favourable opinion was given. Further information on annual reporting requirements to RECs can be found: <http://www.hra.nhs.uk/resources/during-and-after-your-study/progress-and-safety-reporting/>   * 1. **Serious Breaches**   Serious Breaches in CTIMPs must be notified to the MHRA, in accordance with their guidance, which can be found here: <https://www.gov.uk/good-clinical-practice-for-clinical-trials> Please refer to *SOP\_018 Management of Breaches in Research* for full details of how to process breaches at UHBW.   1. **End of trial**   The MHRA (where applicable) and the REC must be notified that a trial has ended, within 90 days of the end of the trial, using a *Declaration of End of Trial Form*. Following that, an *end of trial study report* must be submitted to the MHRA (where applicable) and the REC within a year of the end of the study. See <https://www.gov.uk/clinical-trials-for-medicines-manage-your-authorisation-report-safety-issues#end-of-trial> and <http://www.hra.nhs.uk/research-community/end-of-study-and-beyond/notifying-the-end-of-study/> for details of both of these processes.  Where UHBW is sponsor, each of these must be agreed by UHBW R&D department prior to submission. A minimum of two weeks prior to the submission deadline, the report/form must be submitted to [R&Dsponsorship@uhbw.nhs.uk](mailto:R&Dsponsorship@uhbw.nhs.uk), so that the sponsor can agree and authorise submission.  **8.1 Publishing results on the European Clinical trials Database (EudraCT)**  For CTIMPs, in accordance with the commission’s guidelines it is mandatory for the sponsor to post trial results in EudraCT: <http://ec.europa.eu/health//sites/health/files/files/eudralex/vol-10/2012_302-03/2012_302-03_en.pdf>  Where UHBW is sponsor, preparing these results will be delegated to applicable personnel within the research team. Please note that the format for publishing results is stringent and CIs are advised to consider this in developing protocols, data management and statistics plans.   * 1. **Reporting to funder**   Depending on the funding arrangements, a report may need to be submitted at the end of the study to the funder. Information about the format and deadline for the report will be provided by the funder. Please note the CI should ensure the sponsor receives a copy of any report that is submitted.   * 1. **Disseminating results**   In line with the UK Policy Framework for Health & Social Care Research, research results should be disseminated to participants (where possible) and to the scientific community. This is in order to promote research transparency and reduce duplication of research.   1. **Related documents:**  * SOP\_002 Research Sponsorship at UHBW * SOP\_003 Developing and Designing Your Study UHBW * SOP\_009 Research Safety Reporting UHBW * SOP\_007 Research Training UHBW * SOP\_008 Investigator Oversight of Research * SOP\_010 Monitoring and Oversight of Research UHBW * SOP\_017 Confirmation of Capacity and Capability to Deliver Research at UHBW * SOP\_018 Management of Breaches in Research UHBW * SOP\_019 UHBW sponsored research amendments * TMPL\_056 File note template | |
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