Humber Health Partnership

Management of SOPs

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This page details the version history and the main changes made for each new version.

Version Log		
Version number and date	**Author**	**Details of significant changes**
Version 1, 27.10.10	J Pacynko	First SOP approved by R&D Committee on 27.10.10
Version 2, 12.07.12	J Pacynko	SOP amended to simplify the process of review, approval and implementation of SOPs. Also that SOP is available on the HEY R&D website.
Version 3, 20.02.14	J Pacynko	At the end of March and September an email will be sent to research staff reminding them of updates to SOPs in the previous 6 months and asking them to sign an SOP Updates Training Record Links and appendices up-dated
Version 4, 13.11.14	J Pacynko	Page 5 Review and up-dating - SOPs will be assigned a review date 3 years after the approval or previous review date. The review date has been changed from 18mths to 3yrs to be in-line with Trust policy CP001 Development and management of procedural documents policy.
Version 5, 31.01.18	J Pacynko S Moffat	**Changes are shown by wording in red.** ● In abbreviations section: SSA deleted, SSF deleted, HRA IB and RSI added. ● Sending of global email removed and replaced with 6-monthly signing of Training Record to inform research staff of up-dates to SOPs. ● Improved definitions of TMF and REC. ● SOP updates will now be sent out to research staff approximately every 6 months, previously updates were being sent in March and September but some flexibility is required in case no SOPs had been up-dated within 6 months. ● Removal of Appendix 1 and 4 ● Checking and updating of hyperlinks in the UK Clinical Trials Standards (Appendix 3)
Version 6, 14.12.22	G Constable S Moffat	Check and update of links throughout the document. Section 2 – Preparation and version control, page 4 addition of: “ SOPs in development will be saved on the Y drive in Y:\Research\GCP SOPs & forms\SOPs and saved in the following format, R&D GCP SOP [number] [short title] and the words ‘draft’. The draft will be saved in the “Next draft version” folder until it has been reviewed, approved and signed off when it will be moved to the “Current” folder.” Section 2 – Preparation and version control, page 5 addition of : “The final draft of the SOP will be sent for review and comments to the R&D Director.”

		Section 3 – Approval and version control, page 5 addition of: "The R&D Director and R&D QA staff will be given 2 weeks to feedback any comments to the author." "The R&D Director and Manager will then be sent the page 1 of the SOP via Docusign to approve as the current version." "The signature page and the current version of the SOP will be filed in "Current" folder for the relevant SOP." Section 4 – Review and up-dating, page 5 addition of: "SOPs will be assigned a review date 3 years after the approval or previous review date. The new review date will be added to the SOP tab of QA Master Sheet to remind R&D when the review date is due." Section 5 – Dissemination, page 5 change of department name from R&D HEY internet site to RDI HUTH internet site" Section 6 – Training and implementation, page 6 addition of: "Each time an SOP is updated and made available on the RDI website on the HUTH internet site an email will be sent to all research staff asking them to read and digest the changes made." Appendix 1 – Acronyms and definitions, page 7 Addition of e and p prefix, change of HEY to HUTH and updated wording for HRA. Appendix 2 – UK Clinical Trial Standards, page 10 Addition of Medicine for Human Use (Clinical Trial) amendments.
V7	G. Constable L Cox	Sections 1, 2, 3, 4 and 6 - Updated SOP to reflect ICH E6(R3) quality principles, including quality-by-design, critical-to-quality (CtQ) factors, proportionality, data integrity, digital systems governance and oversight expectations Added expectation to consider/document risk-based and data governance impacts when drafting/revising SOPs, and to record these within the version log. Expanded review, approval, dissemination and training requirements to ensure changes to quality-focused/risk-proportionate processes and data integrity expectations are communicated and understood. Update to Group title changed to HHP (Humber Health Partnership.

1 Introduction, purpose and who should use this SOP

- Standard operating procedures (SOPs) are required to formalise and standardise working practices within departments. They are a useful training tool.

- The purpose of this SOP is to describe how R&D SOPs are prepared, approved, reviewed and implemented. This SOP also ensures that the development, approval, review and implementation of R&D SOPs follow a quality-focused, risk-proportionate and fit-for-purpose approach. SOPs must support processes that are designed around critical-to-quality (CtQ) factors, promote data integrity, and enable proportionate oversight throughout the lifecycle of clinical research activities. All R&D staff involved in SOP development must ensure that procedures reflect these principles.

- This SOP should be used by R&D staff when compiling SOPs. Other departments within the Trust may also find this SOP a useful guide.

2 Preparation and version control

- SOPs will be planned and discussed within the R&D Department in order to agree their content and to resolve any queries during drafting.

- During the preparation of SOPs, the ICH E6(R3) quality principles, including identification of critical-to-quality factors, proportionality of procedures, and the need for processes that support data integrity, participant safety, and reliable results. SOPs should be designed using a quality-by-design (QbD) approach, ensuring that procedures are practical, operationally feasible, and aligned with the intended purpose.

- The recommended format of SOPs is to have the following sections; a contents list, introduction, background, purpose, who should use the SOP, details of procedures, acknowledgements, references, appendices.

- The recommended font for SOPs is Arial size 11 with Arial size 9 in Gray-80% in headers and footers.

- Working instruction 01 is a template for SOPs. This is saved on the Y drive in Y:\Research\GCP SOPs & forms\Working instructions.

- Appendix 1 is the list of acronyms and their definitions and is relevant to all R&D GCP SOPs.

- Appendix 2 lists the standards to which clinical trials that investigate the safety and/or efficacy of a medicinal product are conducted. This applies to all the R&D GCP SOPs.

- SOPs in development will be saved on the Y drive in Y:\Research\GCP SOPs & forms\SOPs and saved in the following format, R&D GCP SOP [number] [short title] and the words 'draft'. The draft will be saved in the "Next draft version" folder until it has been reviewed, approved and signed off when it will be moved to the "Current" folder.

- When drafting or revising SOPs, authors must evaluate whether updates are required to reflect changes in risk-based approaches, digital system governance, data management expectations, or oversight responsibilities. Any such considerations should be documented during the drafting process.

- The date in the header will be up-dated on the day the draft is changed. The title of the SOP will also be in the header above the version details.

- The watermark 'DRAFT' will be added to appear on each page of the SOP.

- Each page will be numbered x of y in the footer starting with the cover as page 1.

- When a draft SOP has been completed as fully as possible, it will be forwarded to either the R&D Manager/QA Manager/R&D Monitor (depending on who the author is) for an in depth review. Comments will be incorporated into the draft SOP.

- The final draft of the SOP will be sent for review and comments to the R&D Director.

3 Approval and version control

- The R&D Director and R&D QA staff will be given **2 weeks** to feedback any comments to the author.

- If changes need to be made, the amended final version will be forwarded to the R&D Manager, QA Manager and Monitor for a final review and approval. As part of the approval process, the R&D Director, R&D Manager and QA staff will confirm that the SOP includes proportionality, quality-focused design, and clarity of responsibilities. Approval will ensure that the SOP supports processes that protect participant safety, maintain data integrity, and enable effective oversight throughout the research lifecycle.

- Once approved the watermark 'DRAFT' will be removed and SOPs will be given a version number and a date, starting with version 1 and date of approval.

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- In the header in the top left hand corner of each page of the SOP will be the title of the SOP and underneath the version details, for example:
  R&D GCP SOP 01 - version 1, 23.09.09

- The R&D Director and Manager will then be sent the SOP via Docusign to sign the first page and approve as the current version.

- The approving individuals must ensure that the SOP reflects current regulatory expectations, including the modernised approach to risk-proportionate quality management and data governance.
- The signature page and the current version of the SOP will be filed in the "Current" folder for the relevant SOP.

4 Review and up-dating

- SOPs will be assigned a review date 3 years after the approval or previous review date. The new review date will be added to the SOP tab of QA Master Sheet to remind R&D when the review date is due. As part of each review, the author must assess whether updates are required to maintain alignment with ICH GCP guidance including changes relating to quality-by-design principles, CtQ factors, proportionality, digital systems, data integrity, and oversight responsibilities. The review should consider whether any new risks, regulatory changes, or operational developments necessitate modification of the SOP.

- SOPs may well require updating before the review date due to a change in legislation or change in MHRA/Ethics/HRA requirements or changes in working practices.

- If the SOP is up-dated the version number and date will be up-dated and the version log will be completed on page 2 of the SOP.

- The version log should clearly document the nature of the changes, including enhancements to quality-focused processes, risk-based approaches or data governance requirements.

- When the review date is due the author may decide that there is no update required at that time. The author will note in the version log that the SOP was reviewed and required no change and therefore there was no change of version number and date.

5 Dissemination

- SOPs will be placed on the SOP section of the RDI HHP internet site by the Trust's Web Services department.

- Superseded versions of SOPs will be saved on the Y drive in Y:\Research\GCP SOPs & forms\SOPs.

- A person using a paper copy of an SOP should always check that they have the latest version by checking the R&D internet site. This is stated on the front cover of all SOPs.

6 Training and implementation

- Prior to the start of the study, all research staff involved with the study will be required to read the GCP SOPs and document that they have done so when completing the 'Training method' section of the Training and Delegation Log.
- Likewise, new research staff before becoming involved with the trial, will be required to read the GCP SOPs and document that they have done so when completing the Training and Delegation Log. Training will include awareness of the ICH E6(R3) quality principles, including quality-by-design, critical-to-quality factors, proportionality and data integrity. Staff must understand how these principles influence the design and conduct of research processes.
- SOPs will be implemented by individual researchers after signing the Training and Delegation Log.
- Departmental training on SOPs will be organised upon request.
    - Each time an SOP is updated and made available on the RDI website on the HHP internet site an email will be sent to all research staff asking them to read and digest the changes made.
- Dissemination should highlight changes to quality-focused processes, risk-proportionate procedures and data integrity expectations to ensure staff understand how these updates affect operational practice.

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Appendix 1 - Acronyms and definitions

A more detailed glossary is available at the Clinical Trials Toolkit website
https://www.ct-toolkit.ac.uk/glossary/

AE – Adverse Event: Any untoward medical occurrence in a clinical trial subject administered a medicinal product, medical device or intervention and which does not necessarily have a causal relationship with this treatment.

IB – Investigator Brochure: A document containing a summary of the clinical and non-clinical data relating to an investigational medicinal product. The IB is intended to provide the investigator with information necessary for the safe conduct of the study. The IB is a document of critical importance throughout the drug development process and is updated with new information as it becomes available.

CI – Chief Investigator: The investigator with overall responsibility for the conduct of a multi-site trial. The application for ethical review should be submitted by the CI. The CI is known as the national coordinating investigator on the IRAS application form.

CRFs – Case Report Forms: A printed or electronic document designed to record all of the clinical trial data for each trial subject. Also known as data collection forms. Each subject has a CRF.

CTA – Clinical Trial Authorization: Authorization granted by the MHRA to conduct a clinical study with an IMP.

CTIMPs – Clinical trials which involve investigational medicinal products.

CtQ – Critical to Quality Factors (Protecting Participant Safety, ensuring Data integrity, producing reliable, credible results and supporting ethical and scientifically sound conduct)

e___ - The prefix used to indicate the object is electronic, for example eCRF is an electronic case report form.

EEA – European Economic Area
EU – European Union

GCP – Good Clinical Practice: A standard for the design, conduct, performance, monitoring, auditing, recording, analyses and reporting of clinical trials that provides assurance that the data and reported results are credible and accurate, and that the rights, integrity and confidentiality of trial subjects are protected.

HHP – Hull University Teaching Hospitals NHS Trust: Also known as the Trust.

HRA – Health Research Authority: An NHS organisation established to protect and promote the interests of patients and the public in health research. The National Research Ethics Service (NRES) is now part of the HRA.

ICF – Informed Consent Form: A form signed and dated by a study subject which voluntarily confirms their willingness to participate in a study after having been informed of all relevant aspects of the trial.

ICH – International Conference on Harmonization: The objective of ICH GCP is to provide a unified standard for the EU, Japan and USA to facilitate the mutual acceptance of clinical trial data by the regulatory authorities in these jurisdictions.

IMP – Investigational Medicinal Product: An IMP is a pharmaceutical form of an active substance or placebo being tested or used as a reference in a clinical trial including products:-

- already with a marketing authorisation but used or assembled (formulated or packaged) in a way different from the authorised form.
- used for an authorised indication.
- used to gain further information about an authorised form.

ISF – Investigator Site File: A file kept at the PI's site for organizing and collating all trial documents pertaining to the site. The CRFs form part of the ISF.

MHRA – Medicines and Healthcare products Regulatory Agency: The UK authority that reviews clinical research protocols, pharmacovigilance data and medicinal product license applications. This authority also conducts GCP inspections.

QbD – Quality by design - A systematic, proactive approach to designing clinical trial processes so that quality is built in from the outset. QbD focuses on identifying critical-to-quality factors, anticipating risks, and developing proportionate, practical procedures that protect participant safety and data integrity.

p___ - The prefix used to indicate the object is paper based, for example pISF is a physical investigator site file.

PSF - Pharmacy Site File: A trial specific file located in the Pharmacy Department and used to collate the trial documents relevant to pharmacy.

PI – Principal Investigator: The investigator responsible for the clinical trial at the research site. In a multi-site trial, there should be one PI for each research site. In the case of a single-site trial, there is no Chief Investigator just the Principal Investigator.

QA – Quality Assurance refers to the ongoing monitoring and evaluation of the various aspects of a clinical trial to ensure that standards of quality are being met.

Research Ethics Committee (REC) (also ethics committee) - Committee established to provide participants, researchers, funders, sponsors, employers, care organisations and professionals with an independent opinion on the extent to which proposals for a study comply with recognised ethical standards. For CTIMPs, the ethics committee must be one recognised by the United Kingdom Ethics Committee Authority. The REC undertaking the ethical review of an application is also known as the Main REC.

RSI – **Reference Safety Information** - This is a list of medical events detailing the Serious Adverse Reactions (SARs) that are expected for the IMP which is to be used by sponsors as a reference point when assessing a SAR to determine whether it is a SUSAR. The documents that contain the RSI are the IB for an IMP without marketing authorisation and an SPC for an IMP with marketing authorisation. Both documents have a section that lists the expected adverse reactions for the IMP.

SAE – **Serious Adverse Event** - An adverse event is serious if it; results in death, is life-threatening, requires hospitalization or prolongation of existing hospitalization, results in persistent or significant disability or incapacity, or is a congenital anomaly or birth defect.

SAR – **Serious Adverse Reaction -** A serious adverse event that is either possibly, probably or definitely related to the investigational medicinal product in a study medic's opinion.

SPC – **Summary of Product Characteristics** - The basis of information for health professionals on how to use the medicinal product safely and effectively. They are written and updated by pharmaceutical companies and are based on their research and product knowledge. It is then checked and approved by the UK or European medicines licensing agency.

The leaflet that is included in the pack with a medicine is a patient-friendly version of this document.

SUSAR – Suspected Unexpected Serious Adverse Reaction - An SAE becomes a SUSAR if the event is suspected (possibly, probably or definitely) to be related to the IMP and unexpected for i.e. not previously documented in any of the product information (investigator brochure, SPC, patient information leaflet) or protocol.

TMF – Trial Master File - A file, or series of files, either paper (pTMF) or electronic (eTMF), used to collate **all** the trial documents and enables the conduct of a clinical trial and quality of the data produced to be evaluated by MHRA GCP inspectors. The TMF is the complete history of the trial and will enable the trial to be reconstructed if necessary. The TMF includes the investigator and pharmacy site files as well as the CRFs.

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Appendix 2 – UK Clinical Trial Standards

It is a legal requirement for clinical trials that investigate the safety and/or efficacy of a medicinal product, to be conducted according to the UK Clinical Trial Regulations. ICH GCP is incorporated into the UK CT regulations. The UK Framework for Health and Social Care Research must also be followed for the conduct of all research in the NHS.

These are the standards that need to be adhered to for the conduct of CTIMPs sponsored by Hull University Teaching Hospitals NHS Trust in order to protect the safety of clinical trial participants and produce the highest quality clinical trial data.

See below for a summary and weblinks for these documents.

UK CT regulations are available at http://www.legislation.gov.uk/ by entering the Statutory Instrument number.

- Medicines for Human Use (Clinical Trials) Regulations 2004
  Statutory Instrument 2004/1031 (1 May 2004).Transposed European Directive 2001/20/EC into UK
  law. Known as the Clinical Trials Directive

Implementation of GCP in the conduct of clinical trials on medicinal products for human use
Ethics review system came under law
Each member state has to appoint a competent authority (MHRA in UK)
Additional safety reporting requirements
Amendments required to follow a process

- Medicines for Human Use (Clinical Trials) Amendment Regulations 2006
  Statutory Instrument 2006/1928 (29 Aug 2006). Transposed European Directive 2005/28/EC into UK law.
  Known as the GCP Directive

Principles and detailed guidelines for GCP
Sponsor has overall responsibility – duties can be delegated but not responsibilities
UK specific requirement to report serious breaches
Archiving of TMF

- Medicines for Human Use (Clinical Trials) Amendment no. 2 Regulations 2006
  Statutory Instrument 2006/2984 (12 Dec 2006)

Allows incapacitated adults in certain emergency situations to participate in research without the consent of a legal representative

- Medicines for Human Use (Clinical Trials) and Blood Safety and Quality (Amendment) Regulations 2008
  Statutory Instrument 2008/941 (1 May 2008)

Allows a minor to receive emergency treatment in clinical trials without parental consent in certain circumstances

- The Medicines for Human Use (Miscellaneous Amendments) Regulations 2009

Statutory Instrument 2009/1164 (8 May 2009)
Urgent safety measures – rapid response to public health threats/pandemics e.g. swine flu

- The Medicines for Human Use (Advanced Therapy Medicinal Products and Miscellaneous Amendments) Regulations 2010
  Statutory Instrument 2010/1882 (19 Aug 2010)
Advanced therapy medicinal products – tissue engineered products.

- The Medicines for Human Use Regulations 2012
Statutory Instrument 2012/1916 (14 Aug 2012)
Replaces most of the Medicines Act 1968 and about 200 statutory instruments with a simplified set of rules.
The new regulations set out a comprehensive regime for the authorisation of medicinal products for human use; for the manufacture, import, distribution, sale and supply of those products; for their labelling and advertising; and for pharmacovigilance.

- The Medicines for Human Use (Clinical Trials) (Amendment) (EU Exit) Regulations 2019

ICH GCP is available at http://ichgcp.net/ (first published in 1996)
- International Conference on Harmonisation Good Clinical Practice (E6)

UK Policy Framework for Health and Social Care Research last updated 4th November 2022 is available at
https://www.hra.nhs.uk/planning-and-improving-research/policies-standards-legislation/uk-policy-framework-health-social-care-research/uk-policy-framework-health-and-social-care-research/

ICH Guideline – Guideline for Good Clinical Practice E6 (R3) – Adopted 6th January 2025 – New guidelines effective as of the 28th April 2026. For further information - https://www.gov.uk/government/collections/medicines-clinical-trials or HRA Website - https://www.hra.nhs.uk/