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**Trial Master File Contents**

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| **TMF section** | **Document(s)** | **Use either an ‘X’, if held in main TMF, or ‘N/A’ or name of the responsible department to indicate where the documentation is held** | **Use a ‘P’ or an ‘E’ to indicate if the document is paper or electronic format** |
| --- | --- | --- | --- |
| **Section 1: Trial Information and Contact Details** |
| **1.1** **Trial information** | * Full and short study title
* R&D number
* IRAS number
* Portfolio/CPMS number
* EudraCT number
* Funder’s reference number
* Name, address and phone number of Chief Investigator
* Name, address and phone number of the trials unit
* Name and address of sponsor
* List of trial sites and contact details for key personnel
 |  |  |
| **Section 2: Funding** |
| **2.1****Grant application and costings** | * Final submitted grant application
 |  |  |
| **2.2****Grant award / funding letter** | * Original grant/funding award letter issued by the trial funder
 |  |  |
| **2.3** **Invoices and payments** | * Invoices received from sites and collaborators and invoices sent to funder
* File Note to indicate where invoices are held (e.g. trials unit/R&D /UHBW Finance) and that UHBW Finance holds records of invoices received and payments made on its Invoice Approval System. Income received by the Trust is captured on UHBW Finance’s general ledger
 |  |  |
| **2.4** **Funding correspondence**  | * Correspondence with the Funder. If this information is held in the Contracts section, please indicate here
 |  |  |
| **Section 3: Sponsorship** |
| **3.1****Sponsorship request form** | * Sponsorship request form and associated correspondence with sponsor
 |  |  |
| **3.2** **Sponsor study risk assessment** | * Current signed sponsor study risk assessment and superseded versions
 |  |  |
| **3.3****Study Set Up and Management Plan** | * Current signed Study Set up and Management Plan and superseded versions
 |  |  |
| **3.4** **Sponsorship letter and Statement of Responsibilities** | * Sponsorship letter
* Signed Statement of Responsibilities
 |  |  |
| **3.5****Set up correspondence with sponsor and any other sponsorship-related issues**  | * Correspondence with sponsor relating to the set up of the trial and any correspondence with the sponsor after study set up concerning sponsorship issues
 |  |  |
| **Section 4: Approvals and Permissions** |
| **4.1** **NIHR portfolio adoption** | * Confirmation of NIHR portfolio adoption
 |  |  |
| **4.2** **HRA approvals** | * Statement of Activities / Organisation Information Document
* Schedule of Events / Schedule of Events Cost Attribution Template
* HRA initial assessment letter and final approval letter
* Evidence of registration on a public database
* Correspondence with HRA
 |  |  |
| **4.3** **REC approvals** | * REC acknowledgement of receipt of application
* Initial REC response/provisional opinion and response to REC
* Final REC favourable opinion letter (including REC membership list)
* Other correspondence with REC
 |  |  |
| **4.4****MHRA approvals** | * Completed Clinical Trial Application (CTA) form and cover letter
* MHRA acknowledgement of receipt of CTA
* Initial MHRA response to CTA and response to the MHRA
* Final MHRA approval of the trial
* Other correspondence with the MHRA
 |  |  |
| **4.5****Other agency approvals** | * Other agency approvals e.g., GTAC, CAG, HSIC
 |  |  |
| **4.6****Sponsor permission to greenlight sites** | * Sponsor permission to main study team to greenlight sites
 |  |  |
| **Section 5: Amendments** |
| **5.1****Amendments**  | * Sponsor authorisation of proposed amendment (CTIMP amendment assessment form) and associated documents
* Signed amendment application and associated documents
* Acknowledgement of receipt of amendment from the HRA/REC/MHRA
* Any correspondence with the HRA/REC/MHRA regarding further information about the amendment and copies of any updated documentation
* Initial and final approval letters/emails from the HRA/REC/MHRA (as applicable)
* Amendment version control log
 |  |  |
| **Section 6: Trial Documents** |
| **6.1****Protocol** | * Current trial protocol and superseded versions
* Protocol CI signature page for current and superseded versions of protocol
 |  |  |
| **6.2****Participant information leaflet (PIL), informed consent form (ICF), invitation letter and any other written information to patients** | * Current trial participant information leaflet (s) and superseded versions, including translations (as applicable)
* Current trial informed consent form(s) and superseded versions, including translations (as applicable)
* Participant invitation letter(s) and superseded versions
* Any other documentation given to trial subject (including advertisements for subjects)
 |  |  |
| **6.3** **GP letter** | * Current and superseded versions of the letter(s) issued to trial participants’ GP
 |  |  |
| **6.4****Case Report Form(s) (CRF)** | * Current CRF templates and superseded versions
* Current CRFs version control form (as applicable e.g. if using multiple CRFs with different version numbers)
* Any study specific SOP or guidance on processing CRFs
 |  |  |
| **6.5****Indemnity certificates** | * Clinical trial indemnity certificates and/or insurance statements for the duration of the trial
 |  |  |
| **Section 7: Agreements and Variations to Agreements** |
| **7.1****Agreements and variations to agreements** | * Funding agreement and variations to agreement (or indicate if filed elsewhere e.g. in Funding section)
* Collaboration agreement and variations to agreement
* IMP supply agreement(s) with the IMP manufacturer(s)
* Site agreement template and version control log
* Site agreements and variations to agreement (or indicate if filed elsewhere e.g. in Site section)
* Material transfer agreements and variations to agreement
* Licence agreements (for the use of licensed tests or assessments)
* Any other agreements e.g. user/confidentiality agreements and service level agreements (SLAs)
* Sponsor’s vendor suitability assessment (if applicable)
 |  |  |
| **Section 8: Investigational Medicinal Product (IMP)**  |
| **8.1****Investigator Brochure (IB) / Summary of Product Characteristics (SmPC)** | * Current IB or SmPC for each IMP and non-IMP used in the trial and superseded versions
 |  |  |
| **8.2****Reference Safety Information**  | * Current approved Reference Safety Information and superseded versions (refer to 8.1 as necessary)
 |  |  |
| **8.3****IMP label(s)** | * Label(s) used for the trial IMP(s)
 |  |  |
| **8.4****Prescription template** | * Prescription temp
 |  |  |
| **8.5****QP release**  | * Certificate of analysis (batch release certificate) issued by the Qualified Person (QP) for each batch of the trial IMP(s) throughout the trial
 |  |  |
| **8.6****Handling and storage of IMP** | * Study specific pharmacy procedures and guidance, including risk assessments and pharmacy manuals for sites
* Contact details for IMP manufacturer and/or distributor
 |  |  |
| **8.7****Monitoring and Quality**  | * IMP storage temperature records
* QP reports and assessments
* Stability data

  |  |  |
| **8.8** **Records of unblinding** | * Documentation and correspondence relating to unblinding of participants
 |  |  |
| **8.9****Shipping**  | * SOPs or guidance relating to the shipping of trial IMP(s) from central distributor to sites
* Shipping records of IMP from central distributor to sites
* Shipping records of site-to-site transfer of trial IMP(s)
 |  |  |
| **8.10****Site IMP accountability** | * SOPs or guidance relating to accountability processes for IMP(s) held at trial sites
* IMP accountability at each site (collate at end of trial)
 |  |  |
| **8.11** **Central IMP accountability** | * SOPs or guidance relating to central IMP accountability processes (as applicable)
* Emails, correspondence and meeting minutes relating to any central IMP accountability issues arising throughout the trial
 |  |  |
| **8.12****Destruction** | * SOPs for the destruction of trial IMP(s) at the end of the trial
* Destruction accountability at each site (collate at end of trial)
* Destruction accountability at central distribution site (collate at end of trial)
* Documentation relating to IMP destruction during the course of the trial
 |  |  |
| **Section 9: Devices**  |
| **9.1****Devices** | * Evidence of CE marking
* Application to MHRA and MHRA approval letter (if falls under the regulations)
* Product description and operating instructions
* Equipment testing
 |  |  |
| **Section 10: Trial Management** |
| **10.1****Trial Standard Operating Procedures (SOPs)** | * A list of all trial-specific SOPs
* A copy of all current trial-specific SOPs and superseded versions
* Identification of location of R&D SOPs and/or trial unit SOPs (as applicable)
 |  |  |
| **10.2****Trial Management Group (TMG), Independent Data Monitoring Committee (IDMC) and Trial Steering Committee (TSC)** | * Trial Management Group
	+ Terms of Reference or Charter, list of members and signed agreements from each member
	+ Agenda, papers and correspondence relating to all meetings
* Trial Steering Group
	+ Terms of Reference or Charter, list of members and signed agreements from each member
	+ Agenda, papers and correspondence relating to all meetings
* Independent Data Monitoring Committee
	+ Charter, list of members and signed agreements from each member
	+ Agenda, papers and correspondence relating to all meetings
* IDMC reports, including interim reports required for the statistical analysis
 |  |  |
| **10.3****Main study team training**  | * Trial delegation log for main study team
* CVs and GCP training
* Training log for main study team
* Study-specific training
 |  |  |
| **10.4****Verification of trial records (EDGE)** | * Sponsor’s documented annual verification of the trial records held on EDGE
 |  |  |
| **10.5****General communications** | * Trial newsletters
 |  |  |
| **Section 11: Sites – (***If documentation is held in separate Trial Site Files (TSFs) , this should be clearly flagged below)* |
| **General** |
| **11.1****Site documentation (e.g. templates)**  | * Site feasibility assessment form template
* Local application pack sent to sites
* Training materials
* Evidence that sites provided with approved documentation for amendments
* Investigator site file index template
* Site delegation log template
* Subject identification code list
 |  |  |
| **Site Specific****(documentation required for each site)** |
| **11.2****Feasibility** | * Sponsor feasibility assessment (and Expression of Interest where applicable)
 |  |  |
| **11.3****Site confirmation of Capacity and Capability** | * Site confirmation of Capacity and Capability to take part in the study
 |  |  |
| **11.4****Site initiation and greenlight**  | * Site Initiation Visit (SIV) – including SIV report, training materials and correspondence with sites
* Completed greenlight checklist
* Greenlight email to sites and copy to sponsor
 |  |  |
| **11.5****Site IMP updates** | * Evidence that sites informed in a timely manner of any IMP safety issues and updates to IMP
 |  |  |
| **11.6** **Site training** | * Trial specific training log
* CVs and GCP certificates
 |  |  |
| **11.7****Completed CRFs** | * Signed, dated and completed paper case report forms (CRFs) (as applicable)
* Data queries and documentation of corrections to CRFs
 |  |  |
| **11.8****Completed questionnaires and/or diaries** | * Completed patient reported outcome measures
 |  |  |
| **11.9****General site documentation and correspondence** | * Site staff delegation log
* Authorised users log for access to trial database
* Documentation that site provided with SAE reporting templates and guidelines for completing SAEs
* Site confirmation of continuing Capacity & Capability (where provided)
* Any other site-specific correspondence, e.g. regarding site set up, or any site-specific issues
 |  |  |
| **11.10****Site close down** | * Site close down visit report
* Evidence that all outstanding actions completed
* Site close down letter
* Permission for site to proceed to archiving
 |  |  |
| **Section 12: Screening and Recruitment** |
| **12.1****Screening enrolment log** | * Current and superseded versions of the screening enrolment log template
* Current and superseded versions of the completed screening enrolment log
* Any SOP or guidance related to the participant screening enrolment process
 |  |  |
| **12.2****Randomisation**  | * Any SOPs or guidance related to trial-specific randomisation
* Master randomisation list (or 3rd party contact details if applicable)
 |  |  |
| **12.3****Unblinding procedure**  | * Any SOPs or guidance detailing the unblinding procedure for the trial
 |  |  |
| **12.4****Consent** | * Completed consent forms for trial participants (as applicable)
* Any SOPs or guidance relating to the consent process which is trial-specific
 |  |  |
| **Section 13: Data Management**  |
| **13.1****Data Management Plan** | * Current Data Management Plan (including evidence of computer systems validation and processes for database sign off and release, version control and data lock) and any superseded versions
 |  |  |
| **13.2****Data management** | * Database metadata
* SOPs for management of data cleaning and corrections
* Authorised personnel list for making changes to central database
* Routine and triggered data management reports
 |  |  |
| **13.3** **Database**  | * Database specification
* Documentation of database user acceptance testing and sign off
* Confirmation of database lock
* Dataset extracted from the locked database
* Any SOPs or guidance relating to database management
* Database unlocking (as applicable)
 |  |  |
| **13.4****Computer systems validation** | * Evidence of computer systems validation (hardware and software)
 |  |  |
| **13.5****Statistics** | * Statistical Analysis Plan
* Any SOPs relating to the statistical arrangements for the trial
* Correspondence relating to the statistical analysis
 |  |  |
| **13.6****Publications** | * Trial publication plan
* Any papers published during the trial and a copy of the first trial publication made after the end of the trial
 |  |  |
| **Section 14: Laboratories** |
| **14.1****Accreditation, certification, quality control or other validation** | * Any SOPs or guidance relating to laboratory tests validation processes
* Accreditation, certification, quality control or other validation of medical/laboratory/technical procedures/tests, including any updates to document competence of facility to perform required test(s) and support reliability of results
 |  |  |
| **14.2** **Normal/reference value(s)/range(s)** | * Normal/reference value(s)/range(s) for medical/laboratory/ technical procedure(s) and/or test(s) which are not referenced in the protocol and any updates
 |  |  |
| **14.3****Trial samples** | * Any SOPs or guidance relating to the management and processing of human tissue samples
* Documentation that human samples collected specifically for the purposes of the trial have been disposed of according to ethics authorisation (as applicable)
* Record of retained body fluids/tissue samples (if any)
 |  |  |
| **Section 15: Breaches and Pharmacovigilance**  |
| **15.1** **Protocol deviations****and GCP non-compliances** | * Trial protocol deviations log (including temperature excursions)
* Correspondence relating to the resolution of protocol deviations (including CAPAs and reporting to regulatory authorities (as applicable)
* Any trial specific SOPs relating to breaches
* Any other correspondence relating to protocol deviations and GCP non-compliance
 |  |  |
| **15.2****Pharmacovigilance SOPs** | * Any trial-specific SOPs relating to pharmacovigilance
 |  |  |
| **15.3** **SAE reporting** | * Serious Adverse Event (SAE) reports and follow up reports
* Correspondence relating to SAEs
 |  |  |
| **15.4****SUSAR reporting** | * SUSAR reports submitted to the MHRA and to REC and any correspondence between the MHRA, REC, sponsor and site
* Confirmation of the date REC was informed and the date the MHRA was informed via the eSUSAR website
* Confirmation that the SUSAR has been resolved/closed
 |  |  |
| **15.5****SSAR listings** | * SSAR (Suspected Serious Adverse Reaction) listings
 |  |  |
| **Section 16: Monitoring**  |
| **16.1****Trial monitoring plan** | * The sponsor’s current monitoring plan and any superseded versions
* Trial unit’s monitoring plan (as applicable)
* Any trial-specific SOPs or guidance relating to trial monitoring
 |  |  |
| **16.2****Site monitoring reports** | * Site specific monitoring reports, actions and evidence that all actions resolved
 |  |  |
| **Section 17: Annual Reporting** |
| **17.1****Development Safety Update Report and Annual Safety Report** | * Finalised Development Safety Update Reports (DSURs)
* Cover letter sent to MHRA with the DSUR
* MHRA acknowledgement of receipt of DSUR
* MHRA acceptance of DSUR (as applicable)
* Any other correspondence with the MHRA
* Annual Safety Reports (ASRs) submitted to ethics
* REC acknowledgement of ASR
 |  |  |
| **17.2** **Annual Progress Report**  | * Finalised Annual Progress Reports (APRs)
* Cover letter sent to REC with APR (as applicable)
* REC acknowledgement of receipt of APR
* REC acceptance of APR
* Any other correspondence with the REC
 |  |  |
| **17.3** **Reports to funder**  | * Annual reports to funder
 |  |  |
| **17.4****General correspondence** | * General correspondence
 |  |  |
| **Section 18: End of Study** |
| **18.1****Close down**  | * Confirmation from sponsor that may proceed to submit End of Study Declaration
* End of Study Declaration form
* Documentary evidence of submission of End of Study Declaration form to the REC and to the MHRA
* Any correspondence with external, contracted parties (such as IMP suppliers, the HSCIC or other data providers and licence providers) regarding the closure of the trial
* Completed sponsor close-down visit checklist and documentation that all follow up actions completed
 |  |  |
| **18.2** **Final reporting** | * Final reports to ethics, MHRA (EudraCT) and funder
* Acknowledgement of receipt of reports from ethics, MHRA and funder
 |  |  |