**Appendix 3**

**Quality Technical Agreement (QTA) Template**

QUALITY TECHNICAL AGREEMENT

**FOR THE MANUFACTURE, OVERLABELLING , IMPORTATION, RELEASE AND DISTRIBUTION OF INVESTIGATIONAL MEDICINAL PRODUCTS (IMPs) FOR PRODUCT NAME / TRIAL REFERENCE**

REFERENCE NUMBER

Between

SPONSOR ORGANISATION

And

MANUFACTURING ORGANISATION

And

IMPORTING ORGANISATION

This template has been provided by The Newcastle upon Tyne Hospitals NHS Foundation Trust Quality Assurance (QA) Pharmacy team for queries regarding the content/use may be directed to [anne.black7@nhs.net](mailto:anne.black7@nhs.net).

QUALITY TECHNICAL AGREEMENT

FOR THE MANUFACTURE, OVERLABELLING , IMPORTATION, RELEASE AND DISTRIBUTION

OF INVESTIGATIONAL MEDICINAL PRODUCTS (IMPs) FOR PRODUCT NAME / TRIAL REFERENCE

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**QUALITY TECHNICAL AGREEMENT**

This Technical Agreement is made between:

**SPONSOR (Contract Giver; CG)**

<<Sponsor Address>>

<<Sponsor Address>>

<<Sponsor Address>>

<<Sponsor Address>>

and

**MANUFACTURER (Contract Acceptor – Manufacture; CAM)**

<<Manufacturer Address>>

<<Manufacturer Address>>

<<Manufacturer Address>>

<<Manufacturer Address>>

and

**IMPORTER (Contract Acceptor – Import; CAI)**

<<Importer Address>>

<<Importer Address>>

<<Importer Address>>

<<Importer Address>>

# Definitions

“Drug Products or DP” shall mean Investigational Medicinal Products (IMP), as further defined in Appendix 1 of this agreement.

“GMP” shall mean all current good manufacturing practices applicable to pharmaceuticals in Great Britain, as may be applicable to the manufacturing of DP for use in clinical trials.

“GDP” shall mean all current good distribution practices applicable to pharmaceuticals in Great Britain, as may be applicable to the storage and distribution of DP.

“Quality or Technical Agreement” shall mean this Agreement describing the allocation between the parties of roles and responsibilities relating to quality and operational responsibilities with regard to the provision of the Drug Products.

# Scope of agreement

This Technical Agreement defines the roles and responsibilities between the CG and CAM and CAI in ensuring compliance with GMP, GDP and the Medicines for Human Use (Clinical Trials) Regulation 2004 (SI 2004:1031) as amended, with regard to the provision of pharmaceutical services as specified in Appendix 1: Drug products and services.

Allparties will strictly observe the detailed pharmaceutical responsibilities which are specified in

Appendix 2: Responsibilities of each Party.

All parties must appoint Contact Persons as named in Appendix 3: Key Contact Persons.

# Regulatory information

The parties acknowledge that CG shall be the Sponsor of the relevant clinical trial. Thus, will perform all the obligations and responsibilities of a CG as set out in ICH Good Clinical Practice Guidelines and the Medicine for Human Use (Clinical Trials) Regulations 2004 (SI 2004/1031) as amended from time to time.

The CG shall ensure that the clinical trial is conducted according to all applicable legal requirements and in accordance with established ethical, medical and scientific standards, including without limitation the ICH requirements for Good Clinical Practice and the Declaration of Helsinki 1996. The CG shall obtain, or procure that other trial sites shall obtain, appropriate clinical trial authorisation from the relevant Competent Authorities for the use of the Drug Products in the clinical trial as per the applicable and relevant guidelines, directive, statute and regulations.

The CG shall ensure that the trial is approved by the relevant research ethics committee(s) before the trial commences.

The CG bears the sole responsibility for the use of the Drug Products in clinical trials independent from the localisation of execution, except for liability arising from the acts or omissions of other parties such as failure to manufacture or distribute the Drug Product in accordance with GMP or GDP or inherent defects or errors in the manufacture of the Drug Product.

CAM and CAI have the full capability and appropriate licences for manufacture, packaging, labelling and QP release, importation including QP oversight of the Drug Product(s) as described in Appendix 1 of this agreement and as required for this clinical trial. Any wholesaling, manufacturing, packaging, labelling and distribution services will be at all times processed and controlled in compliance with the appropriate regulations, where applicable, for Good Manufacturing Practices, Good Distribution Practices, Good Clinical Practices for medicinal products for human use.

# Deviations

CAM and CAI must without delay notify the CG in writing of all deviations from procedures or specifications that can be of any risk to the safety of the patient or the quality of the product.

Results of any investigations and a proposal for corrective and preventive actions to be taken must be provided in writing to the CG. The documentation will be retained as part of the Batch Documentation for the batch affected.

# The Technical Agreement (including termination)

This Agreement becomes effective on the date of the final signature and shall remain valid up to 5 years (“Term”). This agreement will be reviewed and updated every five (5) years unless the parties agree to amend the agreement prior to this with mutual consent, in writing.

Any variances from this Agreement must be in writing and approved by all Parties to this Agreement.

Each party may terminate this Agreement at 3 (three) months’ notice in written form to the other party.

Termination of this Agreement, however caused, shall not prejudice or affect any rights, action or remedy which shall have accrued before termination or shall accrue thereafter to any party.

This Agreement may not be assigned, modified or amended except in writing signed by duly authorised representatives of all parties.

This Agreement and its Appendices shall be made available to the relevant authorities in the concerned countries upon their request.

This Agreement must be executed in triplicate originals with each Party retaining one original for its records. Each party agrees to deliver to the other all such documents and information as may be required for the other party to perform its obligations under this Agreement.

# Importation

Following manufacture and QP certification by CAM, CAI will import the IMP and perform the requisite QP oversight that the IMP has been QP certified in a listed country before making the IMP available to sites. The specific responsibilities of the QPs at CAM and CAI may be summarised in a separate agreement between the two parties as required by the quality systems of both parties.

# Temperature Excursions

CAM is responsible for transportation of IMP from CAM site to CAI site. Any temperature excursions which occur up to the point of delivery to CAI is the responsibility of CAM and the impact of this excursion must be assessed by CAM with notification of outcome to CAI and CG.

CAI and CAM are jointly responsible for assessing the impact of temperature excursions during storage at CAI and onward transportation to trial sites. The outcome must be notified to CG.

CG is responsible for assessment of temperature excursions following delivery of IMP to site. CAM and/or CAI should assist CG in determining the impact of any excursion through the provision of stability data.

# Documentation Practices

Completed documentation will be archived in accordance with current regulatory guidance and retained for a period of at least 5 (five) years after completion or formal discontinuation of the last clinical trial in which the batch was used. This documentation includes, but is not limited to the following:

* Batch manufacturing records
* Release records
* Deviation reports
* Secondary documentation-i.e. environmental monitoring results, validation data, calibration, cleaning records, maintenance records and complaint investigations data

# Quality Control/Assurance

*CAM and CAI* holds a Manufacturer’s Licence from the MHRA (UK), or relevant competent authority, for the manufacture of Investigational Medicinal Products (IMP’s) authorising activity relevant to that being performed under this agreement.

All starting materials must be sourced from a bona fide Manufacturer or Wholesaler holding a Wholesale Distribution Authorisation (for Human Medicinal Products)

Release of each batch of product must be under the authority of an authorised QP. Importation from a listed country must be performed under the oversight of an authorised QP.

CAM and CAI must maintain a suitable Pharmaceutical Quality System.

CAM must provide QP Certificates of Batch Release for each batch supplied, along with appropriate Certification to both CG and CAI for each batch certified. CAI must provide evidence of completion of the requisite QP oversight checks for each batch imported to CG.

# 

# Complaints

Any complaint from CG regarding quality of supplied product must be acknowledged by *CAM and/or CAI* within 2 working days.

A report containing details of the investigation with corrective and preventative actions must be forwarded to CG within 30 working days. *CAM and CAI* must make every effort to complete investigations and provide feedback including actions assigned to CG in a timely manner.

# Recall and Returns

CAM and CAI must notify CG of any issue which may result in recall or near miss relating to the drug product(s) specified in this Agreement, including any starting materials.

CG must co-ordinate and document the recall process and is responsible for co-ordination and disposal of all products returned by sites. CAM and CAI must cooperate and facilitate any recall decision by CG.

CAM and CAI maintains the right to notify the relevant regulatory authority of potential recall situations where they believe this is the correct course of action but is not agreed by the CG.

# Audit

CG or their representative is entitled to conduct a routine audit of CAM and CAI facilities relevant for the services detailed in this agreement on a 2 yearly basis. Dates for routine audits should be mutually agreed at least 4 weeks in advance.

# Confidentiality

The information contained in this agreement is confidential and must not be divulged to any other party without the permission of all signatories.

# Final Provision

Amendments to this Quality Technical Agreement and its Annexes may only be carried out by mutual consent and shall be made in writing. Any amendments to the appendices 1 to 7 may be signed for CG by a responsible Quality representative and together with the signature of CA the annexes will be binding upon the parties.

### 

### Appendix 1

### Drug products and services

This version of the Technical Agreement covers the project scope as detailed below:

Trial: ***Trial Name/Description***

**Supply of drug products:**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **NAME OF IMP** | **THERAPY** | **MANUFACTURER** | **PACKAGING** | **STORAGE CONDITIONS** | **QUANTITY** |
|  |  |  |  |  |  |
|  |  |  |  |  |  |
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### Appendix 2

### Responsibilities of each Party

|  |  |  |  |
| --- | --- | --- | --- |
| **Regulatory** | **CG** | **CAM** | **CAI** |
| Approve the technical agreement | **X** | **X** | **X** |
| Supply regulatory and trial specific documents required for product specification file (PSF) | **X** |  |  |
| Obtain Clinical Trial Authorisation with competent authorities | **X** |  |  |
| Notify regulatory authority of changes to licences/documentation relevant to manufacture/testing of the products | **X** |  |  |
| Maintain and archive the product specification file |  | **X** |  |
| Managing of investigating centers | **X** |  |  |
| Authorisation for MHRA to access PSF relevant to the trial |  | **X** |  |
| Maintain PSF for all IMPs within the clinical trial |  | **X** |  |
| Supply of information for updates to IMPDs | **X** | **X** | **X** |
| **Drug Products** | | | |
| Procurement and manufacture of placebo drug products |  | **X** |  |
| Procurement and manufacture of drug products |  | **X** |  |
| Generating the Release Documents (e.g. Certificates of Analysis / QP Certification / QP Oversight) for all drug products in compliance with the responsibilities defined in the QP to QP agreement |  | **X** | **X** |
| Insured transportation of all drug products to CAI |  | **X** | **X** |
| **Packaging Materials** | | | |
| Procurement of packaging materials |  | **X** |  |
| Vendor approval (packaging materials) |  | **X** |  |
| Assembly of drug products and packaging materials |  | **X** |  |
| Storage of drug products |  | **X** | **X** |
| **Release of Drug Products** | | | |
| Provide copies of approval from authorities and ethical committees, IMPD file and other relevant information | **X** |  |  |
| Control of finished drug products |  | **X** |  |
| Technical release |  | **X** |  |
| Green light for shipping/regulatory release | **X** |  |  |
| Provide QP release certificate for finished drug products to CG and CAI |  | **X** |  |
| Perform QP Oversight activity on receipt of necessary documentation from CAM |  |  | **X** |
| Use and compliance of drug products within Clinical Trials Authorisation | **X** |  |  |

|  |  |  |  |
| --- | --- | --- | --- |
| **Out of Specification Investigations** | | | |
| Out of specification investigation | **X** | **X** |  |
| Out of specification approval/rejection | **X** | **X** |  |
| **Documentation** | | | |
| Archiving original batch documents for at least 5 (five) years after completion or formal discontinuation of the last clinical trial in which the batch was used | **X** | **X** | **X** |
| Retention of relevant documentation according to EC 2003/94/EC | **X** | **X** | **X** |
| Sample Retention |  | **X** |  |
| **Destruction** | | | |
| Not destroy materials or records (those not controlled under records retention policies) without the permission of the CG |  | **X** | **X** |
| Destruction of defective products that remain at CAM |  | **X** |  |
| Destruction of remaining products (at the end of the study) that remain at CAI |  |  | **X** |
| Authorisation for, and confirmation of, destruction of remaining products (at the end of the study) at investigational sites | **X** |  |  |
| **Logistics** | | | |
| Responsible for providing information concerning special requirements for packaging and monitoring supplies during shipment |  | **X** | **X** |
| Determination of storage conditions for drug products |  | **X** |  |
| Vendor approval of logistics provider for shipment of IMP from CAM to CAI |  | **X** |  |
| Shipping of finished products from CAM to CAI |  | **X** |  |
| Supply of temperature monitoring data for shipping of finished products (if applicable) to investigational sites |  | **X** |  |
| Assessment of deviations during transport to CAI |  | **X** |  |
| Storage and management of stock at CAI |  |  | **X** |
| Vendor approval of logistics provider for shipment of IMP from CAI to Sites |  |  | **X** |
| Storage and management of stock at investigational sites | **X** |  |  |
| Shipping requests for finished drug products | **X** |  |  |
| Preparation of shipping documents for shipping of drug products from CAM to CAI |  | **X** |  |
| Preparation of shipping documents for shipping of finished DP to investigational sites |  |  | **X** |
| Shipping of finished products to the investigational sites |  |  | **X** |
| Supply of temperature monitoring data for shipping of finished products (if applicable) to investigational sites |  |  | **X** |
| Assessment of deviations during transport to investigational sites |  |  | **X** |

|  |  |  |  |
| --- | --- | --- | --- |
| **Complaints and Drug Products recall** | | | |
| Inform other parties within 2 working days of any information that will likely lead to a product recall | **X** | **X** | **X** |
| Make available relevant information to assist in investigations relating to product recalls. | **X** | **X** | **X** |
| Administering, documenting and facilitating any product recall arising in any circumstances | **X** | **X** | **X** |
| Communication with authorities | **X** |  |  |
| Monitoring of product recalls | **X** |  |  |
| DP recall decision / Termination of clinical trial | **X** |  |  |
| Receiving, collecting and administering any Adverse Reactions (ARs) suffered by patients, which are or may possibly be due to the product. | **X** |  |  |
| Investigation of complaints related to manufacturing or product quality | **X** | **X** |  |
| **Handling of any product returns** | | | |
| Storage in an appropriately controlled, dedicated area |  | **X** | **X** |
| Keep inventory records of any inadvertently returned IMP received | **X** | **X** | **X** |
| **Change Control** | | | |
| Notification of all major changes to DP & process (e.g. changes in raw/packaging materials, suppliers, manufacturing processes, test methods, etc.) |  | **X** |  |
| Approval of all major changes to DP & process | **X** |  |  |
| Update of relevant documents affected by changes | **X** | **X** | **X** |
| **Quality Audits and Auditing** | | | |
| Permit CG or its representatives to audit the manufacturing or importation site (specific to the products covered in this agreement) providing at least four (4) weeks’ notice is given. |  | **X** | **X** |
| Permit regulatory authorities to audit the site. | **X** | **X** | **X** |
| Inform all parties of regulatory audits and observations relevant to the products covered in this agreement. | **X** | **X** | **X** |
| Selection and audit of vendors (sub-contracted parties) for IMP manufacture, packaging and importation via a formally documented vendor-approval process | **X** | **X** | **X** |
| Supply of appropriate documentation requested by CG to enable approval of selected vendors for IMP manufacture, packaging and import |  | **X** | **X** |
| Approval of selected vendors for IMP manufacture, packaging and importation | **X** |  |  |

### 

### Appendix 3

### Key Contact Persons

CG

|  |  |  |  |
| --- | --- | --- | --- |
| Name | Designation | Contact number | E-mail |
|  |  |  |  |
|  |  |  |  |

CAI

|  |  |  |  |
| --- | --- | --- | --- |
| Name | Designation | Contact Number | E-mail |
|  |  |  |  |
|  |  |  |  |
|  |  |  |  |

**CAM**

|  |  |  |  |
| --- | --- | --- | --- |
| Name | Designation | Contact Number | E-mail |
|  |  |  |  |
|  |  |  |  |
|  |  |  |  |

### 

### Appendix 4

### List of Subcontractors

*e.g. Couriers, Contingency partners and Contract Laboratories*

|  |  |
| --- | --- |
| **CAM Subcontractors** | |
|  |  |
|  |  |

*e.g. Couriers, Contingency partners and Contract Laboratories*

|  |  |
| --- | --- |
| **CAI Subcontractors** | |
|  |  |
|  |  |

### 

### Appendix 5

### Technical Agreement Approval

**Agreed on behalf of the CG**

|  |  |
| --- | --- |
| Name: | Name: |
| Title: | Title: |
| Signature: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ | Signature: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ |
| Date: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ | Date: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ |

**Agreed on behalf of CAI**

|  |  |
| --- | --- |
| Name: | Name: |
| Title: | Title: |
| Signature: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ | Signature: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ |
| Date: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ | Date: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ |

**Agreed on behalf of CAM**

|  |  |
| --- | --- |
| Name: | Name: |
| Title:  (QA Representative) | Title: |
| Signature: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ | Signature: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ |
| Date: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ | Date: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ |

### 

### Appendix 6

### Version History

|  |  |  |
| --- | --- | --- |
| **Version Number** | **Date of Amendment** | **Amendment(s) Made** |
| 1 | DD/MMM/YYYY | First Issue |
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