BARTS HEALTH NHS TRUST PHARMACY CLINICAL TRIALS INFORMATION FOR SPONSORS PACK

Dear:

Date:

Thank you for considering/choosing to conduct your clinical trial at our facility. The purpose of this information pack is to support understanding of local processes for pharmacy setup of clinical trials involving investigational medicinal products (CTIMPs), IMP management and other related activities for all sites within Barts Health NHS Trust.

We encourage you to raise any queries with the pharmacy clinical trials team regarding the processes outlined in this pack prior to site initiation. Otherwise acknowledgement of this pack will be taken as acceptance of the clinical trials pharmacy processes at Barts Health NHS Trust.

1. Barts Health NHS Trust

Barts Health NHS Trust has a long history of research excellence and collaboration in the conduct of clinical trials. This includes strong partnerships with Queen Mary University London and the National Institute for Health Research - as well as charitable, national and international organisations. Barts Health NHS Trust consists of the following hospitals - St Bartholomew's, Royal London, Whipps Cross, Mile End and Newham.

2. Pharmacy Clinical Trials Team

The Pharmacy Clinical Trials Department at Barts Health NHS Trust is an established service delivering high quality pharmaceutical research in accordance with Good Clinical Practice (GCP) and the EU Clinical Trials Directive.

The team consists of dedicated staff including specialist clinical trial pharmacists, pharmacy technicians and assistants. Staff receive training in GCP and have relevant experience in the management of clinical trials and compliance with GCP.

Please see **Appendix A** for the Pharmacy Clinical Trials Team contact details at each site.

3. Feasibility Review Process

All studies to be conducted at Barts Health NHS Trust need to be submitted to the North Thames Clinical Research Network (CRN) for feasibility review. In order for clinical trials pharmacy to initiate local assessment for Capacity and Capability, the sponsor has to send the full document set (including the ones below) via the Principal Investigator, Research & Development office and Local CRN (sss.crnnorththames@nihr.ac.uk). If you are seeking to initiate multiple sites within Barts Health NHS Trust, please also notify the CRN as a separate pharmacy feasibility form will need to be completed for the respective sites.

4. Pharmacy Greenlight Process

Pharmacy (local) clinical trial setup process involves a feasibility review, preparation of Pharmacy Site File and subsequent issue of a Pharmacy Greenlight once all requested documents and information are in place.

Refer to **Appendix B** for a list of documents required for Pharmacy Greenlight.

In addition, pharmacy clinical trials team require the following from sponsor/Clinical Research Organisation:

- Contact details of the main research nurse/manager involved with study setup.

- Pharmacy Site File (hard copy) and latest electronic version of essential documents **at least 2 to 3 weeks prior** to Site Initiation Visit (SIV). Please note that the study file will be re-arranged as per standard Barts Health NHS Trust Pharmacy Clinical Trial Site File Contents Page (**Appendix C**). All other documents not stated on the contents page will be filed in the “miscellaneous” section.

- Pharmacy SIV date to be arranged. Pharmacy SIV may need to be re-arranged in the event where pertinent documents are outstanding.

- Anticipated start date of recruitment, and an update if the date changes.

Overall, this will enable pharmacy to complete and approve internal trial specific documents in readiness for the SIV. For example risk assessments, screening/dispensing/compounding/checking standard operating procedures, blinding plans, out of pharmacy storage assessments, worksheets, prescriptions, labels, accountability/inventory logs, IMP/NIMP management plans, transfer documents, training manuals, change controls, etc.

5. IMP Management

Pharmacy clinical trials team require thorough information, in an IMP/pharmacy manual or other document(s), on the following processes for the IMP(s):

- initial and subsequent ordering
- receipt at site, packaging, storage, stability
- dispensing schedules (i.e. how often dispensing occurs)
- administration
- returns
- destruction

Please find further information about aspects of our involvement in Frequently Asked Questions (**Appendix D**).

Appendix A: Pharmacy Clinical Trials Team Contact Sheet

	St Barts Hospital	Royal London Hospital (& trials at Mile End Hospital)	Whipps Cross Hospital (& trials at Newham Hospital)
Email Address	Clinicaltrials@bartshealth.nhs.uk	RLH_pharmacyCT@bartshealth.nhs.uk	Christopher.Abbott@bartshealth.nhs.uk
Telephone Number	**Dispensary Oral Drugs** 020 3465 5250 **Chemotherapy Production Unit Drugs** *(aseptically prepared drugs)* 020 346 56670	020 3594 6680	0208 539 5522 x 6353
IMP Delivery & Correspondence Address	**Dispensary Oral Drugs** Pharmacy Clinical Trials Team Basement, Inpatient Pharmacy King George V Building St Bartholomew's Hospital London EC1A 7BE **Chemotherapy Production Unit (CPU)** Pharmacy Clinical Trials Team Pharmacy Chemotherapy Unit, 7th floor, King George V Building St Bartholomew's Hospital London EC1A 7BE If the study is a combination study at St Barts Hospital i.e. dispensary and CPU then: there is a preference for *both addresses* to be used i.e. dispensary IMP(s) sent to the dispensary address and CPU IMP(s) sent to CPU address. If this is not possible then the Chemotherapy Production Unit address must be used.	Pharmacy Clinical Trials Team Old Outpatients Building The Royal London Hospital Stepney Way London E1 1BB	Pharmacy Clinical Trials Team Pharmacy department Outpatients building Whipps Cross Hospital, Whipps Cross Road, Leytonstone London E11 1NR

Each trial will have a Lead Technician and Lead Pharmacist assigned to the trial. You will be provided with these contact details at the site selection stage.

IMP must never be sent to the Principal Investigator or to any other address other than the above pharmacy addresses.

Appendix B: Documents Required for Pharmacy Greenlight

The following are <u>essential</u> for Pharmacy Greenlight

- Original and subsequent MHRA approval Letters
- Original and subsequent Ethics Approval Letters
- HRA approval Letter
- MHRA Clinical Trial Application
- Clinical Advisory Group Letter (Oncology Studies Only)
- Protocol
- Investigator Brochure/Summary Product Characteristic
- MHRA Approved Labels
- Marketing authorisation*****
- Interactive Web Response System (IWRS) Manual/ Log on Details (if required)*
- Signed Delegation Log (including pharmacy personnel)*****
- Study Specific Contact Information
- Pharmacy Manual*****
- Qualified Person (QP) release*****
- Transmissible Spongiform Encephalopathies (TSE) statement for all IMPs*****
- Material Safety Data Sheet for all IMPs*****
- Certificate of Analysis*****
- Qualified Person (QP) Declaration *****

*at the pharmacist's discretion Pharmacy Greenlight can be given if this document is not required or expected to follow at a later stage.

Pharmacy Site File Contents

Trial Name:	EudraCT number:	Site:

Behind Contents	Monitoring Log & Contact Information Charge Sheet File Note Log Document Change Log
1	Clinical Trial Summary Sheet Pharmacy Training Log
2	Delegation Log
3	Master Prescription
4	Labels
5	Patient LOG
6	CUMULATIVE Accountability Log
7	SUBJECT SPECIFIC Accountability Log
8	Destruction forms
9	IMP ordering and delivery Delivery notes QP release/batch certificate Order forms
10	Protocol Pharmacy Manual
11	All Approval Letters – MHRA, HRA, REC and C&C
12	Contract
13	Feasibility Review
14	Temperature Records: Central Location File Note Excursion information Deviation form
15	Trial Specific training SIV slides (if applicable) CV & GCP certificates – Central location file note
16	Amendment forms
17	IBs/SmPC
18	Correspondence
19	Miscellaneous
20	Superseded documents

Appendix D: Frequently Asked Question

Accountability

Sponsor Accountability Logs are not used. Standardised Cumulative and Subjective Accountability Logs are used. Refer to **Appendix E** Pharmacy Clinical Trials Cumulative Accountability Log & **Appendix F** Pharmacy Clinical Trials Subject Specific Accountability Log.

For Chemotherapy Production Unit trials Cumulative Accountability Logs are used; subject specific detail dispensing is recorded on the Chemotherapy Production Unit Worksheets. Barts Health NHS Trust Pharmacy team do not enter IMP accountability on IXRS post dispensing or returns. If this is a requirement then this is to be completed and arranged with the research team.

Archiving

The pharmacy site file is archived together with the main site file once the study has been closed as per Barts Health NHS Trust policy and national guidelines.

Aseptic Preparation

This applies to all trials involving IMP(s) which require reconstitution or preparation under validated aseptic conditions. The aseptic facility is a licensed unit. The minimum turnaround time for IMPs made in the Chemotherapy Production Unit is 2 hours. More complex IMPs may take longer. If permitted by protocol, doses may be made in advance of dosing day based on expiry time of prepared IMP; they are not released to the patient until bloods/critical tests have been reviewed.

Doses made at Barts Hospital that are required to be transported to Royal London hospital require a 4 hour transport and preparation time (not including the administration time) The shut-down for routine deep cleaning is arranged at specific weekends and therefore no impact to the conduct of this study would be anticipated.

Delegation Log

The designated Lead Clinical Trials Pharmacist and Pharmacy Technician will be added on to the main study delegation log at SIV. All additional pharmacy staff involved in the trial will read trial specific SOP and complete a trial specific pharmacy training log.

Destruction

All sites have a preference for returns to be reconciled by monitor and courier arranged for offsite destruction. However, local destruction is possible at all site (except Whipps Cross Hospital) and chargeable.

Destruction of Used Injectables

Barts Health NHS Trust does not retain or accept used syringes or injection pens for any studies. All used syringes and injectable pens are destroyed immediately after use within the aseptic unit and/or on the ward/clinic area. Royal London site accepts empty vials for non-hazardous substances.

IWRS Access for Receipt of IMP

As many members of Barts Health NHS Trust Clinical trials team should have access as possible to enable cover for sick leave/holidays etc. At a minimum, the assigned clinical trial technician and three back up members should be provided with IWRS access.

IWRS Access Dispensing Notifications

Royal London: where blinding permits, the nursing and research team receive the IWRS notifications and attach to the trial prescription for pharmacy.
Whipps Cross: as above.
Barts Hospital: where blinding permits, the nursing and research team receive the IWRS dispensing notifications and email these to the Barts Hospital generic (group) mailbox for the chemotherapy production team or for the dispensary.

Labels for Dispensing

Patient name and hospital number is added to the IMP labels. This is for patient safety reasons.

Monitoring Visits

Monitoring visits must be booked with a minimum of 2 weeks notice. Visits can be booked for a maximum of two hours only unless prior arrangement is made with the trial technician. Visits longer than 2 hours are subject to charges as per individual study contract. Barts Health NHS Trust Clinical Trials Pharmacy does not encourage remote monitoring due to pertinent resources required.

Out of Hours Service

There is no out of hours pharmacy clinical trials service available at Barts Health. As a result, all unblinding activities must be managed by the PI and research team.

Prescription Formats

Royal London: paper prescriptions are used**.** Authorised sample prescriptions are filed in the pharmacy file.
Whipps Cross: paper prescriptions are used**.** Authorised sample prescriptions are filed in the pharmacy file.
Barts Hospital: ARIA electronic prescribing is used for the oncology prescriptions; the ARIA oncology prescriptions are built and checked by the pharmacy team and further validated by the principal investigator. The ARIA oncology prescriptions are not printed and filed in the pharmacy file. The ARIA prescriptions can be accessed and viewed with the research team. Other specialities use paper prescriptions.

Randomisation

Pharmacy is generally not involved in randomisation of patients to arms or kits, except in the case where pharmacy is unblinded for the purposes of the study. This must be discussed and agreed prior to SIV taking place. Randomisation/kit allocation is usually done by the Research teams/nursing staff using the IWRS systems.

Retention of IMP Packaging

All pharmacy sites do not retain empty packaging for any IMPs in Pharmacy at Barts Health NHS Trust. Due to the volume of IMP that are processed on a daily basis the clinical trials pharmacy cannot retain any packaging for monitor verification.

Returns

Barts Health NHS Trust can only receive and reconcile patient returns in the form of oral tablets or capsules. Oral drugs classed as cytotoxic or 'handle with care' will only be reconciled if in blister packs. Pharmacy cannot receive any items part administered, attached to IV lines or containing sharps. Used vials, syringes, injection pens and/or the packaging of such items are not retained.

Staff Training Records and GCP

All Pharmacy staff are given training on GCP. GCP Certificates are NIHR approved with 2 years validity. GCP certificates and CVs will not be placed in individual trial folders; these are filed centrally and available to review upon request

Stock

Minimal stock is to be delivered to the site to ensure sufficient space for all trials. Decision on initial order quantities are to be held prior to SIV. Initial shipments will only be accepted once the SIV has taken place. Clinical trial technicians and clinical trial assistants will check if received stock is in the correct conditions and is suitable for use.

Standard Operating Procedures

The following site specific SOPS are available to view on request from sites:

- Archiving of Pharmacy Clinical Trial Records
- Investigational Medicinal Products Disposal or Destruction
- Quarantine of IMP
- Temperature monitoring, excursion and storage of Clinical Trial materials and IMPs

Additionally, each trial has a trial specific dispensing procedure designed and approved by the pharmacy clinical trials team. Pharmacy staff members involved in the trial may self-train by reading and following steps in the dispensing procedure. This training is documented by signing the clinical trial pharmacy training log**.**

Storage Facilities

All IMPs at each site are stored in a secure, temperature controlled area that requires badge/code access. The room temperature is kept between 15 – 25 Degrees Celsius. The fridge temperature is kept between 2 – 8 Degrees Celsius. An assessment is required at the feasibility stage on storage due to limited space and numbers of fridges/freezers at each site.

All sites have annual calibration to ensure the calibration and maintenance of the pharmacy equipment are performed. Calibration certificates are kept at each site. In the event of a power failure all sites have back-up generators. IMPs can be moved to back-up fridges.

All IMPs are explicitly stored in pharmacy. If IMPs are required to be stored outside of pharmacy (e.g. at ward/clinic level) then an out of storage risk assessment and sponsor agreement is completed by pharmacy for each IMP.

TempTales

Barts Health NHS Trust clinical trial pharmacy do not retain TempTales. TempTales received with deliveries are downloaded and the summary graph is printed on receipt and filed. If the TempTale is a temperature indicator, rather than a downloadable device a photocopy will be filed. Temperature excursions outside of the acceptable temperature range will be reported to the monitor by the clinical trial pharmacists and/or technicians.

Temperature Monitoring

Royal London: daily minimum-maximum manual reading recorded on working days only. Audible alarm during working hours only and no out hours alarm notification. Calibration certificates are available on site.

Whipps Cross: minimum-maximum manual reading recorded daily (including weekends). Calibration certificates are available on site.

Barts Hospital: for dispensary based IMPs there is a minimum-maximum manual reading recorded daily (including weekends). Calibration certificates are available on site. The Chemotherapy Production Unit have an electronic temperature recording system - Pharmagraph. The sensor takes a reading every minute. In the event of an excursion an alarm sounds. Temperature data is routinely printed and filed by the pharmacy technician.

Un-blinding/Code break

Barts Health NHS Trust pharmacy clinical trials service does not include code break or un-blinding of treatment and therefore must be handled by clinical research staff. The final decision to un-blind a patients' treatment should be made by the PI and/or Medical Monitor. There is no out of hours pharmacy service available for clinical trials.

Appendix E: Clinical Trial Pharmacy Cumulative Accountability Log

Clinical Trial Pharmacy Accountability Log – CUMULATIVE

Trial Name:	**IMP name (strength and form):**	Unit (eg 1 vial, 1x30 tablets):
EudraCT number:	Trust:	Site name/number:
Principal investigator:	Sponsor:	

					IN		OUT				BALANCE		CRA CHECK	
Date	Activity Type *(Receipt, dispensing, return, destruction, quarantine)*	Batch / LOT number	Expiry Date	BOX ID / KIT ID	Shipment Number	Number of Units RECEIVED	Subject initials	Subject Trial number	Number of units DISPENSED *(if applicable)*	Number of units DESTROYED *(disposed, returned, quarantined, if applicable)*	Number of units in stock Previous page balance____	Entry made by / check by *(initials)*	Sign and date	Comments
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Clinical Trial Pharmacist/Technician Signature:	Date:	Monitor Signature:	Date:

Appendix F: Clinical Trial Pharmacy Subject Specific Accountability Log

Clinical Trial Pharmacy Accountability Log – SUBJECT SPECIFIC

Trial Name:	IMP name (strength and form):	Unit (eg 1 vial, 1x30 tablets):
EudraCT number:	Trust:	Site name/number:
Principal investigator:	Sponsor:	
Subject Number:	Subject Initials:	Date of Birth:

DISPENSING							RETURNS			CRA CHECK	
Date	Visit	Batch / LOT number	Expiry Date	BOX ID / KIT ID	Number of dose units dispensed	Dispensed/ checked by	Date	Quantity of dose units returned	Entry made by *(initials)*	Sign and Date	Comments
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Clinical Trial Pharmacist/Technician Signature:	Date:	Monitor Signature:	Date:

NIHR CRN North Thames: CRNForm/07- Clinical Trial Pharmacy Accountability Log SUBJECT SPECIFIC – Version 1, 03.04.2017 Page _____ of _____

Version	Date	Written By	Approved by	Comments
1	16/5/18	Aidan O'Callaghan	Anh Nguyen	N/A
2	15/10/18	Aidan O'Callaghan	Lola Babalola	Minor format changes, temperature monitoring clarified for all sites