STANDARD OPERATING PROCEDURE 27
Management of Investigational Medicinal Products (IMPs) for Clinical Trials

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Version 3.0	8 March 2024	Biennial review: Updates to web links. New process flowchart for IMP supply. Addition of information relating to quarantining of IMP stock.
Version 2.0	17 November 2021	Biennial review: Change to new format. Amended title to Management of IMP. New sections on IMP returns and destruction, IMP stability and shelf-life extension and co-enrolment added.
Version 1.5	24 July 2019	Biennial review: Addition of further information on the regulatory release procedure. Other minor text updates
Version 1.4	27 July 2016	Biennial review: Reference to use of MHRA's Grey Guide and new section on non-IMPs added. Clarification of when supplies should be sent to sites and of labelling requirements.
Version 1.3	9 June 2014	Biennial review: Title amended to include 'Storage,' plus inclusion of IMP storage requirements.
Version 1.2	26 March 2012	Format change to comply with SOP 1.
Version 1.1	26 March 2010	Addition of details regarding transfer of IMP(s) between sites (section 3.3.5).
Version 1.0	26 March 2008	

STANDARD OPERATING PROCEDURE 27
Management of Investigational Medicinal Products (IMPs) for Clinical Trials

1. Purpose and Scope

This Standard Operating Procedure (SOP) describes the management process for the supply, storage, and destruction of Investigational Medicinal Product(s) (IMPs) and how IMPs must be labelled according to the requirements of the Medicines for Human Use (Clinical Trials) Regulations 2004 and EU Directive 2003/94/EC.

This SOP focuses on IMP activities that University of Warwick (UoW) staff and investigational sites may undertake and therefore is not an exhaustive SOP to cover all aspects concerning IMPs in clinical trials.

It is applicable to all University of Warwick staff involved in Clinical Trials of Investigational Medicinal Products (CTIMPs) and to staff working on externally sponsored trials where use of UoW SOPs has been agreed.

Chapter 6 of the Medicine and Healthcare products Regulatory Agency (MHRA) Good Clinical Practice Guide (grey book) has further information on all aspects of IMP management, and it is recommended that staff involved in conducting CTIMPs become familiar with the requirements stipulated in this publication.

A risk appropriate approach to IMP management should be implemented to reflect both the risk to the participant and/or trial integrity of the research carried out, as well as to the risk related to the reliability of trial results. For further information and guidance, refer to section 4.3 'IMP management' in the guide entitled Risk proportionate approaches in clinical trials.

2. Definitions

Investigational Medicinal Product (IMP)	A pharmaceutical form of an active ingredient or placebo being tested or used as a reference in a clinical trial, including a product with a marketing authorisation when used or assembled (formulated or packaged) in a way different from the approved form, or when used for an unapproved indication, or when used to gain further information about an approved use.
Clinical Trial of an Investigational Medicinal Product (CTIMP)	Any investigation in human subjects intended to discover or verify the clinical, pharmacological and/or other pharmacodynamic effects of an investigational product(s), and/or to identify any adverse reactions to an investigational product(s), and/or to study absorption, distribution, metabolism, and excretion of an investigational product(s) with the object of ascertaining its safety and/or efficacy.
Qualified Person (QP)	An individual trained by a recognised professional body who will certify each batch of IMP has been manufactured in accordance with Good Manufacturing Practice (GMP) and meets the conditions of the clinical trial authorisation and the product specification file, prior to despatch to research sites.

3. Background

All clinical trials of IMPs are legally required to comply with International Conference on Harmonisation Good Clinical Practice (ICH GCP) guidelines, the Medicines for Human Use (Clinical Trials) Regulations 2004 and associated amendments.

Chapter 6 of the Medicines for Human Use (Clinical Trials) Regulations 2004 details the requirements for the manufacture and importation of IMPs. The regulations require that IMPs used in clinical trials are manufactured to EU Good Manufacturing Practice (GMP) standards and that GCP is adhered to.

ICH GCP sections 5.12 (Information on Investigational Products); 5.13 (Manufacturing, Packaging, Labelling and Coding of Investigational Products) and 5.14 (Supplying and Handling Investigational Products) explain the sponsor's responsibilities regarding IMPs. These responsibilities may be delegated by the sponsor to Warwick Clinical Trials Unit (WCTU) or other registered clinical trials unit. All delegated duties must be agreed and documented.

The MHRA allows for risk proportionate approaches in clinical trials as it has been observed that in general a 'one size fits all' approach to the design and conduct of trials is not appropriate. This reflects that some trials pose only a minimal additional risk to subject safety and/or trial integrity compared to normal clinical practice, whilst others may have substantial risks.

4. Procedure

4.1 Responsibilities

Chief Investigator (CI) (or delegate)	• Overall responsibility for the management, delivery, storage, use and accountability of IMP(s) as detailed in section 4.6 of ICH GCP entitled "Investigational Products''
Sponsor	• Adherence to ICH GCP sections 5.12 (Information on Investigational Products); 5.13 (Manufacturing, Packaging, Labelling and Coding of Investigational Products) and 5.14 (Supplying and Handling Investigational Products)
Principal Investigator (PI)	• Ensure IMPs are only used in compliance with the approved protocol/trial-specific manual • Provide an explanation on the correct use of the IMP to each trial participant, and check at intervals appropriate for the trial, that each participant is following the instructions properly • Liaise with trial pharmacist to maintain accurate records of the product's delivery to site, use by participants and the return or destruction of the product • Final reconciliation of all IMP related documentation to ensure that all participants were provided the doses specified by the protocol
Pharmacist	• Protocol review to assess practicalities • Maintain accountability logs for receipt, storage, dispensing, return and/or destruction of IMP(s) • Temperature monitoring whilst in storage (if applicable) • Involvement in unblinding procedures (where applicable) • Oversight of local stock management and reordering (where applicable)
Qualified Person (QP)	• The QP must certify each manufactured drug intended for human use prior to its use in a clinical trial. The QP ensures the

	compliance of each batch of Investigational Medicinal Products (IMP), manufactured, or imported, with current requirements.

4.2 When?

The IMP supply and labelling requirements should be determined at the earliest possible stage of the trial design process as the costs need to be included in the grant application.

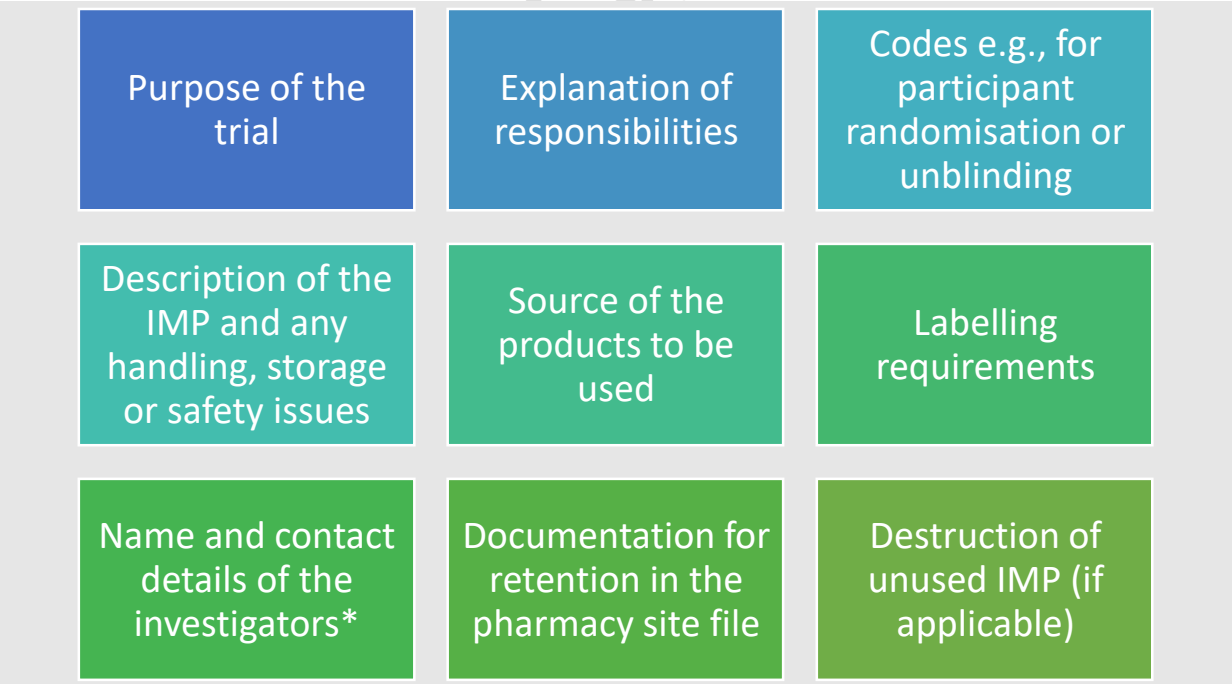
The trial risk assessment and monitoring plan should detail all aspects of IMP management and should be reviewed regularly throughout the course of the trial.

4.3 How?

The CI or delegate should determine the supply, labelling requirements, storage conditions and dispensing procedures for all IMPs in the trial. It is good practice to involve a pharmacist and/or the IMP supplier in these decisions, and to document decisions made and/or actions required.

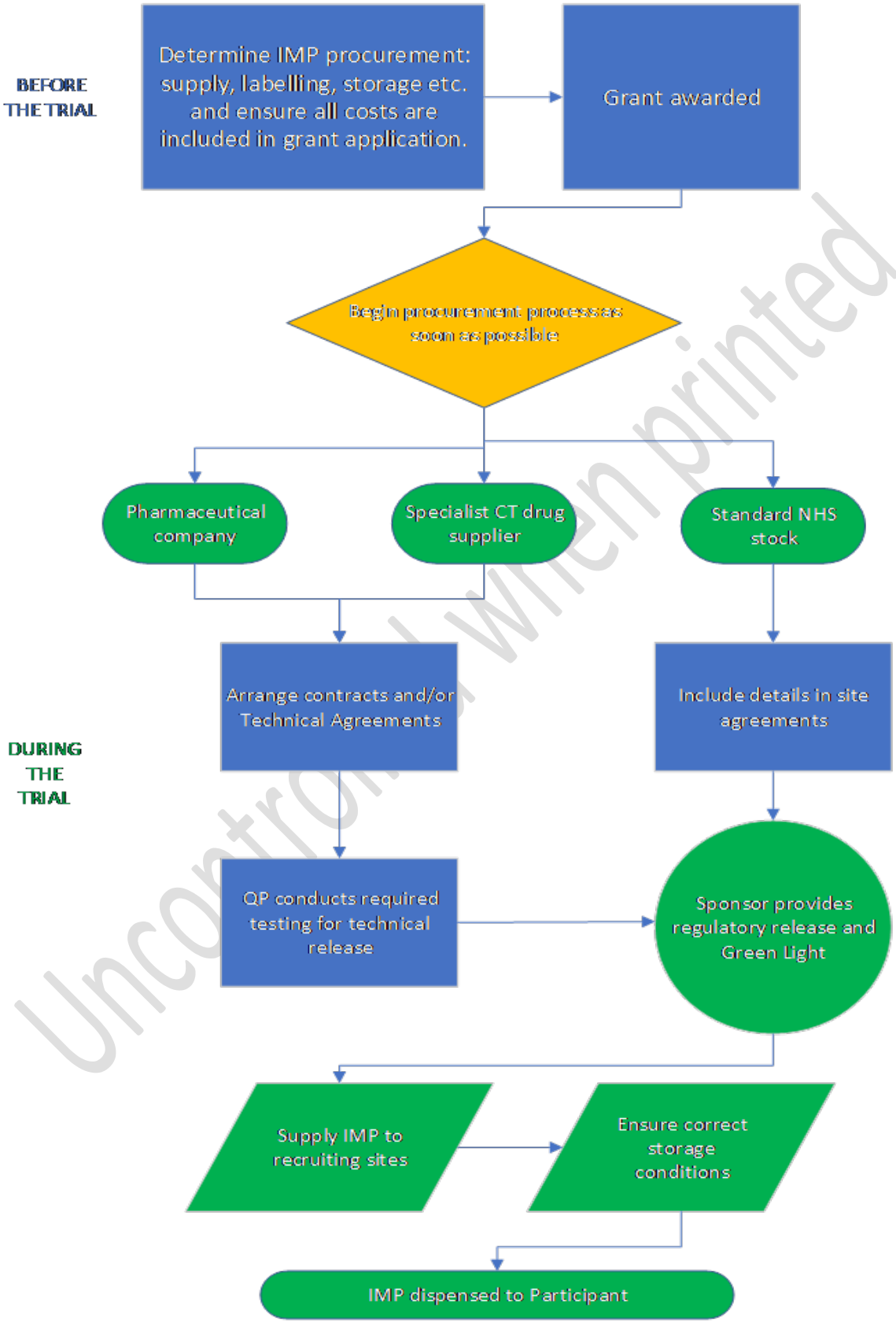
The investigator and/or pharmacist or other appropriate individual should maintain records of the IMP's delivery to the trial site, the inventory at the site, the use by each participant, and the return to the sponsor or alternative disposition of unused product(s). This would usually be documented/available in a Pharmacy Site File (PSF).

Each recruitment site should be properly informed about their responsibilities with respect to the IMP(s) used in the trial. This will usually take place during the site initiation with the pharmacy department and should include:



*And of others involved in the management or administration of the trial

4.3.1 IMP supply



IMP(s) may be obtained directly from a pharmaceutical company, a specialist clinical trial supplier or from standard NHS stock depending on the design of the trial. Any organisation involved in either manufacturing or importing must hold a manufacturing authorisation. In the UK this is a specific manufacturer's/importation authorisation for investigational medicinal products known as the MIA(IMP).

Manufacturing, packaging, and labelling of IMPs for a study may be the responsibility of an IMP supply company with a MIA(IMP) and their responsibilities should be detailed in any contractual agreements.

IMP manufacture and importation must be performed in accordance with the EU 'Rules governing medicinal products in the European Union' (EudraLex Volume 4 – Annex 13). The sponsor retains ultimate responsibility for a trial and must ensure that all aspects required to comply with the clinical trials regulations are in place prior to authorising the start of the trial, however, responsibility for the quality of the IMP is generally delegated to an appropriately qualified person. In the case of University of Warwick sponsored or co-sponsored studies, responsibility for the management of an IMP should be documented on the Division of Sponsor Responsibilities Form. A technical agreement may be required between the sponsor and the delegate to document respective responsibilities for manufacture, storage, shipping, batch certification and testing of the IMPs etc.

(N.B. Some IMP manufacturers based in Europe may have extended summer close down periods which could have repercussions for the trial. Ensure this is considered and discussed at the trial planning phase to make sure that any potential extended lead times are factored into study timelines, and any issues are considered when undertaking the risk assessment.)

Where a clinical trial IMP supply company has been contracted to undertake the manufacturing of the IMP, they will usually be responsible for conducting final batch certification checks before its release. Checks should be completed by the organisation's Qualified Person (QP) to ensure that each batch has been manufactured to Good Manufacturing Practice (GMP) standards and all checks and documentation are in place. This is known as the 'technical release' which is followed by the sponsor (or their delegate e.g., a clinical trials unit) completing a second step, known as the 'regulatory release' or 'regulatory green light,' prior to authorising the commencement of a trial. The authorisation /regulatory green light should be documented by completing the 'Permissions Required to Commence a Randomised Controlled Trial' or 'Green Light Form.' (Template T18 on WCTU SOP templates page).

Regulatory release checks to ensure compliance with regulations will vary depending on the study, but may cover for example:

- Contracts with investigators and any applicable service providers
- If the authorisation of the trial is subject to conditions, that those conditions are met
- Any local or national approvals
- De-coding arrangements are in place (if applicable)

The sponsor (or their delegate) is responsible for ensuring both steps are completed, recorded and the documentation produced is retained in the TMF. These steps are also required for the release of all subsequent batches.

Individual recruitment sites should not be supplied with any trial IMP(s) until the trial 'Green Light' and site specific 'Site Activation Checklist' forms have been completed and signed off by appropriate staff. (Site activation checklist C09).

A sample of each batch of IMP (and placebo, if used) manufactured specifically for a trial should be retained for quality control testing to verify that it is the correct IMP, and the randomisation list has recorded the allocations correctly. See SOP 19 'Quality Control' section 4.3.7 for further details.

4.3.2 Labelling

The requirements for labelling IMP(s) for clinical trials are covered by the Medicines for Human Use (Clinical Trials) Regulations 2004 and EU Directive 2003/94/EC. The MHRA must approve the labels before the trial can start as part of their overall clinical trial approval procedures.

An example label should be sent to the MHRA with the Clinical Trials Authorisation (CTA) application. This sample should include the text of the labelling to be used and be provided in a format representative in terms of size of the label to be used. The labelling requirements for IMP(s) used within and outside of its marketing authorisation are detailed below.

In placebo controlled or blinded trials it is necessary to present all supplies in consistent packaging with consistent labelling to maintain blinding.

Label details should appear in the official language(s) of the country in which the investigational medicinal product is to be used. The particulars listed below should appear on the primary packaging and on the secondary packaging.

4.3.2.1 IMP used within its marketing & importers authorisation (MIA)

For an IMP used within its MIA, the product can be labelled in accordance with the requirements for a dispensed medicine. However, to be consistent with other countries, it is recommended that IMPs are labelled following the guidelines in Annex 13 of GMP.

In practice, this means adding the name of the investigator, trial specific code (e.g., EudraCT number) and trial subject code to the label already in place for the product. The quantity of dosage forms (e.g., tablets, capsules etc.) is generally also added for dispensed medication. An expiry/use-by date is also required and for all products. Some reconstituted products may have a very short usable shelf-life, and this should be made clear.

N.B. The cautionary label "Keep out of reach of children" is a legal requirement on all UK dispensed medicines. Further information is available in Appendix 9 of the British National Formulary (BNF).

Example of label:

Trial (EudraCT number)
Investigator: Dr xxxxxx
Product name, form, and strength
Directions *(as specified by the prescriber)*
Patient name & subject code
Date of Supply: Expiry/Use by date:

Name and address of hospital/primary care supplier **Keep out of reach of children** Any additional cautionary label *(as recommended by the BNF)*

N.B. Exemptions are in place for hospitals and health centres for the assembly/labelling of an investigational medicinal product where the conditions below are satisfied:
(a) the assembly is carried out in—
(i) in a hospital or health centre, and
(ii) by a doctor, a pharmacist or a person acting under the supervision of a pharmacist; and
(b) the investigational medicinal products are assembled exclusively for use in—
(i) that hospital or health centre, or
(ii) any other hospital or health centre which is a trial site for the clinical trial in which the product is to be used.

4.3.2.2 IMP used outside its marketing authorisation

Labelling requirements of IMPs used outside their MIA are stated in Annex 13 of the GMP guidance and should comply with the requirements of Directive 2003/94/EC. The following information should be included on labels, unless its absence can be justified, e.g., use of a centralised electronic randomisation system:

(a) name, address and telephone number of the sponsor, contract research organisation or investigator (the main contact for information on the product, clinical trial, and emergency unblinding)
(b) pharmaceutical dosage form, route of administration, quantity of dosage units, and in the case of open trials, the name/identifier and strength/potency
(c) the batch and/or code number to identify the contents and packaging operation
(d) a trial reference code allowing identification of the trial, site, investigator, and sponsor if not given elsewhere
(e) the trial subject identification number/treatment number and where relevant, the visit number
(f) the name of the investigator (if not included in (a) or (d))
(g) directions for use (reference may be made to a leaflet or other explanatory document intended for the trial subject or person administering the product)
(h) “For clinical trial use only” or similar wording
(i) the storage conditions
(j) period of use (use-by date, expiry date or re-test date as applicable), in month/year format and in a manner that avoids any ambiguity
(k) “keep out of reach of children” except when the product is for use in trials where the product is not taken home by subjects.

Exceptions:
The address and telephone number of the main contact for information on the product, clinical trial and for emergency unblinding need not appear on the label where the subject has been given a leaflet or card which provides these details and has been instructed to keep this in their possession at all times.

Primary and Secondary packaging:
When the product is to be provided to the trial subject or the person administering the medication within a primary package together with secondary packaging that is intended to remain together, and the secondary packaging carries the particulars listed in above, the following information shall be included on the label of the primary package (or any sealed dosing device that contains the primary packaging):
(a) name of sponsor, contract research organisation or investigator
(b) pharmaceutical dosage form, route of administration (may be excluded for oral solid dose forms), quantity of dosage units and in the case of open label trials, the name/identifier and strength/potency
(c) batch and/or code number to identify the contents and packaging operation
(d) a trial reference code allowing identification of the trial, site, investigator, and sponsor if not given elsewhere
(e) the trial subject identification number/treatment number and where relevant, the visit number.

If the primary packaging takes the form of blister packs or small units such as ampoules on which the particulars required above cannot be displayed, secondary packaging should be provided bearing a label with those particulars. The primary packaging should nevertheless contain the following:

(a) name of sponsor, contract research organisation or investigator
(b) route of administration (may be excluded for oral solid dose forms) and in the case of open label trials, the name/identifier and strength/potency
(c) batch and/or code number to identify the contents and packaging operation
(d) a trial reference code allowing identification of the trial, site, investigator, and sponsor if not given elsewhere
(e) the trial subject identification number/treatment number and where relevant, the visit number.

Symbols or pictograms may be included to clarify certain information mentioned above. Additional information, warnings and/or handling instructions may be displayed.

Amendments:
See section 4.3.5 'IMP stability and shelf-life extension' for details of the re-labelling requirements for IMPs if an extension to the 'use-by' date is to be made.

Example of label:

For Clinical Trials Use Only

Trial (EudraCT number)

For use in trial *(give directions for use as stated in patient information leaflet for the trial)*

Investigator: Dr xxxxx

Sponsor: xxxxxx

Product name, form, and strength

Directions *(as specified by the prescriber)*

Patient name and subject code Date of Supply

Use by/Expiry date

Name and address of hospital/primary care supplier **Keep out of reach of children** Any additional cautionary label *(as recommended by the BNF)*

4.3.3 Drug accountability

*If required by trial protocol, otherwise instruct sites to destroy unused IMP according to their local policies.

Each site must maintain records to document shipment, receipt, handling, return and disposal/destruction of used and unused IMP(s). Records should be maintained by investigators to adequately document that the study participants were provided the doses specified by the protocol and to reconcile all IMP(s) received from the sponsor.

However, for drugs already having an MIA (and being used within that MIA) which are supplied via the site pharmacy's local stock; detailing shipment, receipt and return is not applicable.

IMP accountability logs (T06) should be kept for each trial in the Pharmacy Site File (PSF) (T14) to detail:

- Name of site and PI
- Participant identification code
- Date dispensed
- Batch/serial numbers
- Dose
- Quantity dispensed
- Date returned or destroyed*
- Expiration dates
- Quantity returned
- Recorders' initials and date

*As applicable (see 4.3.3.1 and 4.3.8)

If local practices are in place for drug accountability these may be used. However, the trial sponsor should have oversight of this and only approve local procedures if they adequately record all required trial specific information.

4.3.3.1 Returns

If or when a participant returns used or partially used containers to the trial site, accountability of the returns may be performed by the research nurse (or appropriate staff) by entering the data into the Case Report Form (CRF); the containers may then be returned to the pharmacy. Alternatively, the pharmacy may be delegated to perform the accountability checks on returns.

Any IMP returned to pharmacy should be segregated from unused trial stock to avoid its inadvertent use. Under no circumstances should returns be re-used for another participant, as the storage conditions and the integrity of the product cannot always be ensured.

If the IMP is taken off-site by the participant and they decline to return for accountability and destruction, this information should be recorded on the accountability log.

4.3.4 IMP storage and quarantine requirements

ICH GCP section 4.6.4 states that the IMP(s) should be stored as specified by the sponsor and in accordance with applicable regulatory requirements. It is the sponsor's responsibility to determine acceptable storage temperatures, storage conditions (e.g., protection from light) and storage times. The sponsor should inform all involved parties of these determinations and ensure that written procedures are in place to inform the investigators of the handling and storage requirements and the documentation thereof e.g., temperature monitoring requirements (if required), reporting of any temperature excursions to the coordinating centre etc.

A calibrated thermometer must be used by the investigator site to monitor temperature-controlled stock in accordance with MHRA regulations. A copy of the calibration certificate must be provided to WCTU prior to activating a site to start recruitment (C09) and must be retained in the TMF. The investigator site must also retain a copy of the calibration certificate in the investigator and pharmacy site files for monitoring purposes. The investigator site is responsible for re-calibrating thermometer devices in accordance with local policy. Again, for University of Warwick sponsored or co-sponsored studies this responsibility will be delegated via the Division of Sponsor Responsibilities Form.

Ideally, all IMP(s) should be stored and dispensed by pharmacy with access to the stock restricted to authorised personnel only. According to ICH GCP, if appropriate, IMP(s) may be stored in a locked cupboard in other areas e.g., clinics or ward areas as determined by the sponsor or delegate and documented in the protocol as long as it is placed on a dedicated IMP shelf and clearly labelled as belonging to the trial. If storage areas outside the pharmacy are used, these should be assessed to ensure that they are not liable to large daily temperature fluctuations e.g., ensure the product is not stored close to radiators, boilers or other sources of heat, or alternatively that the product is not stored in refrigerators turned down too low, thereby causing the product to freeze.

If a batch of IMP is to be stored in a department separate to pharmacy e.g., Intensive Care Unit for ease of access by clinical team, the sponsor or delegate should ensure adequate oversight of the IMP is in place prior to issuing sponsor green light to commence recruitment. This can include documenting access to the stock is restricted to authorised personnel only, stock is kept segregated from general medical stock, stock is clearly labelled and identifiable to the trial and clear accountability management is in place.

Whenever there is any concern as to the suitability of the IMP for use in humans (e.g., the product was exposed to a temperature excursion, the manufacturer instigates a recall, the IMP has been received by pharmacy prior to Trust approval and pharmacy green light), it must be quarantined until further advice has been given from the manufacturer and the sponsor overseeing the trial. The products should be stored separately in an area clearly labelled as 'quarantine' and discussions held with the sponsor and manufacturer to agree actions. IMP held in quarantine should never be dispensed to participants.

4.3.5 IMP Stability and shelf-life extension

The shelf-life of an IMP should be based on the available stability data for the product. Should an extension to the products shelf-life be anticipated, this may be done at the application stage by putting a proposal defining the criteria based on which the sponsor will extend the shelf-life during an ongoing clinical trial and if this was submitted with the initial or a previous substantial modification filing of the IMP Dossier and has not been questioned by the competent authority, then no substantial amendment would be required.

If the proposal to extend shelf-life based on new stability data is proposed during the trial, defining the criteria based on which the sponsor will extend the shelf-life during an ongoing clinical trial has not been submitted /approved with the initial filing of the IMP Dossier, then a substantial amendment would be required.

If a substantial amendment is required, the Product Specification File would need to undergo a controlled change such that manufacturing sites and the QPs can take appropriate action such as updating labelling instructions, certification criteria etc. IMPs already manufactured, will need to be relabelled. This relabelling will need to be conducted, checked, and documented as per Annex 13 requirements. Paragraph 33 of Annex 13 of the MHRA's Orange Guide (Rules and Guidance for Pharmaceutical Manufacturers and Distributors) deals specifically with this issue. It states:

'If it becomes necessary to change the use-by date, an additional label should be affixed to the investigational medicinal product. This additional label should state the new use-by date and repeat the batch number. It may be superimposed on the old use-by date, but for quality control reasons, not on the original batch number. This operation should be performed at an appropriately authorised manufacturing site. However, when justified, it may be performed at the investigational site by or under the supervision of the clinical trial site pharmacist, or other health care professional in accordance with national regulations. Where this is not possible, it may be performed by the clinical trial monitor(s) who should be appropriately trained. The operation should be performed in accordance with GMP principles, specific and standard operating procedures and under contract, if applicable, and should be checked by a second person. This additional labelling should be properly documented in both the trial documentation and in the batch records.'

4.3.6 Transfer of IMP(s) between research sites

Once an IMP has been delivered to a site it should not subsequently be transferred to another site unless there are exceptional circumstances (e.g., where the safety of a participant is jeopardised if supplies are not provided from another site or if a non-recruiting site was closed down and medication was in short supply). Where transfer does occur, it should be covered by a formal procedure, with clearly documented records of what has been transferred (including quantities, batch numbers, dates, method of transfer etc.). The advice of a QP should be sought to ensure the product is suitable for transfer. Evidence should be held to show that the storage conditions of the product were maintained during shipment. Ideally, the product should be returned to the manufacturer/clinical trial drug supply company for re-labelling, if necessary, and certified by the QP prior to further transfers. Records should be retained in the TMF, and full traceability ensured.

As there are costs involved in any drug pack transfer, this should only be done if there were no other options to ensure supplies are available at a particular site.

The transfer of IMP(s) by an NHS Trust with a central pharmacy to another site within that same NHS Trust, or when a pharmacy of an NHS Trust dispenses an IMP at one of its sites and transfers it to

another of its sites where trial participants are managed is not classified as a site-to-site transfer. However, where either of these activities occurs, there should be a clear formalised procedure in place to ensure the quality of the product (including temperature) is maintained during transit, with documentation of what has been transferred and received, when and by whom.

4.3.7 Non-Investigational Medicinal Products

Products other than the test product, placebo or comparator may be supplied to participants in a trial. Such products may be used as support or escape medication for preventative, diagnostic or therapeutic reasons and/or are needed to ensure that adequate medical care is provided. They are also sometimes used to induce a physiological response.

These products do not fall within the definition of IMP and may be supplied by the trial sponsor or the investigator in accordance with the approved protocol. The quality of the product should be assured and the advice and involvement of a QP is recommended.

4.3.8 Destruction

IMP destruction processes should be clearly described in the protocol. Should any IMP need to be destroyed **during a trial** e.g., due to a temperature excursion or following batch expiry, local procedures may be followed and documented. Similarly, if a batch of IMP is recalled for any reason e.g., after a drug alert from the MHRA defective medicines report centre, the pharmacy department within the recruiting site should follow their local procedures and ensure the PI and trial team are aware of the situation.

For blinded trials where IMP packs which are fully or part-used (particularly controlled drugs) need to be destroyed within a set time period e.g., because of limited storage space at site, considerations should be made regarding maintaining the integrity of the blind against the regulatory requirements and that any decisions must be justified and documented. It is recommended that advice is sought from the QP working on the trial to determine appropriate actions.

The agreed process for the destruction of unused IMP(s) at the **end of a trial** should also be documented in the protocol or trial specific pharmacy instructions manual (which may allow for on-site disposal according to local procedures, or for the participant to dispose themselves).

Once a trial has concluded, the accountability records reconciled, and the used/un-used/returned IMP/placebos have been accounted for, the IMP can be destroyed. If it is an expectation within the protocol that all IMP should be returned by the participant and this does not happen, this should be recorded as a protocol non-compliance

It is good practice however, and if possible, to destroy the IMP only after the clinical trial report has been written which allows for the IMP to be re-reviewed if any discrepancies are identified.

Authorisation for the destruction of trial IMP supply may be required from the sponsor, their delegate, or manufacturer depending on the circumstances, and the person responsible for providing any such authorisation should be documented in the protocol or technical agreement with the drug supply company (as appropriate). Sites should also inform the sponsor of any actions taken if specific sponsor authorisation was not required.

4.3.9 Co-enrolment into other CTIMPs

Co-enrolment is the process of entering participants into more than one study either concurrently or in some cases sequentially. There are no direct statements regarding co-enrolment in the Medicines for Human Use (Clinical Trials) Act SI 2004/1031.

There are several issues that should be considered before co-enrolment is sanctioned, including: study design and statistical considerations; legal and ethical considerations; biological and scientific rationale; participant considerations and logistical and organisational issues.

Plans for co-enrolment should be considered at an early stage of the trial and should be included in the protocol.

In all cases, the safety of study participants, interventions involved, participant burden and the potential impact on the study endpoints must be considered.

It is recommended that a washout period should be defined if there is an intention to allow co-enrolment between studies involving interventions.

Further details can be found in the WCTU protocol writing template for CTIMPs (T16).

List of Abbreviations

BNF	British National Formulary
CI	Chief Investigator
CTIMP	Clinical Trial of an Investigational Medicinal Product
CTA	Clinical Trial Authorisation
ICH	International Conference on Harmonisation
IMP	Investigational Medicinal Product
GCP	Good Clinical Practice
GMP	Good Manufacturing Practice
MIA	Marketing & Importers Authorisation
MHRA	Medicines and Healthcare products Regulatory Agency
PI	Principal Investigator
PSF	Pharmacy Site File
QA	Quality Assurance
QP	Qualified Person
R&IS	Research & Impact Services
SOP	Standard Operating Procedure
TMF	Trial Master File
WCTU	Warwick Clinical Trials Unit

Templates

Template T06	IMP Accountability Log
Template T14	Pharmacy Site File Index
Template T16	CTIMP protocol writing template
Template T18	Green Light RCT Activation form
Checklist C09	Site Activation Checklist