

# Guidance on the content of a pharmacy manual to support clinical trial protocols



This guidance has been produced to help investigators with the content of pharmacy manuals for clinical trials.

We gratefully acknowledge the work of the Trials Units and Research Network Manager (TURN) working group in the development of standardized templates for drug accountability forms.

## Version control

Version 2.0: June 2009

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### Guidance prepared by:

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## 1. Contact details of sponsor

## 2. Trial synopsis

## 3. Study medication

### 3.1. Formulation

For all drugs provide details of the formulation and any excipients included in the preparation<sup>1</sup>.

State which drugs are Investigational Medicinal Products (IMP) according to the CTA.

State which drugs are non Investigational Medicinal Products (NIMP)<sup>2</sup>

### 3.2. Storage

For all drugs specify the storage conditions and the shelf life of the unopened product<sup>1</sup>.

Provide details of the minimum schedule required for monitoring/recording storage conditions and the action to be taken in the event of temperature deviation. Pharmacy departments at local sites will have written standard operating procedures on temperature monitoring.

### 3.3. Labeling/Labels

Provide sample copies of IMP labels.

Provide sample copies of labels for reconstituted products

Provide details of any additional labelling by site eg adding patient ID, local PI, date of dispensing etc to pre-printed IMP labels.

State whether there is any requirement to remove labels and attach to accountability logs?

### 3.4. Reconstitution / Dilution or (Aseptic) preparation

For drugs requiring reconstitution / dilution or (aseptic) preparation give the following information<sup>1</sup>

- Information on the method of reconstitution / dilution or (aseptic) preparation of the IMP.
- Details of the diluents (i.e. WFI, 0.9% sodium chloride) and the container (i.e. infusion bag, bottle) to be used.
- Details of infusion bag size eg 250ml or 500ml
- Details of concentration of infusions.
- Information on the compatibility of the IMP with other drugs and/or infusion equipment, if applicable.
- Details of any special precautions to be taken during reconstitution / dilution or (aseptic) preparation (i.e. use of filters, protection from light).

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<sup>1</sup> For licensed drugs these details can be found in the SPC and other published references. It is acceptable to state "refer to SPC or other published references" for licensed drugs in common use.

<sup>2</sup> See EC Guidance on Investigational Medicinal Products (IMPs) and other medicinal products used in Clinical Trials.

### 3.5. Stability

For drugs requiring reconstitution / dilution or (aseptic) preparation give the following information<sup>1</sup>

- Details of the stability and storage of the reconstituted/ diluted or (aseptically) prepared product.

### 3.6. Administration

Give information on the administration and on any special precautions that need to be taken when administering the drug (i.e. the use of filters, protection from light).

For studies with oral drugs, give information on what to do if a patient misses a dose and information on what to do if a patient vomits a dose.

If applicable give information on how to deal with hypersensitivities. State if local policy can be followed.

Indicate if patient monitoring is required after drug administration.

If available give information on specific treatments for extravasation. Reference can be made to the SPC or local policy.

### 3.7. Ordering & receipt of first and subsequent supplies

List all drugs used in the treatment arms including standard therapy.

Indicate if items such as filters, giving sets, infusion bags are provided.

For each drug indicate;

- Source of the supplies, (e.g. hospital own stock<sup>3</sup>, specific trial supplies free of charge, specific trial supplies at a discounted cost<sup>4</sup>).
- Formulation (e.g. tablet, capsule, solution for injection).
- Dose strength/concentration and size (e.g. 25mg and 100mg capsules, 10mg/ml in 50ml vial).
- Packaging of the supplies<sup>5</sup> (e.g. 35 tablets per bottle, 6 vials per box). Include dimensions if the pharmacy department is expected to store large volumes or bulky supplies.
- Whether or not the drug is an IMP or a NIMP.

For trial specific supplies indicate the supplier, how initial supplies (include quantity) are ordered or whether they are sent automatically and how subsequent supplies (include quantity) are ordered or whether they are sent automatically.

If supplies are specific to an individual patient please specify.

If supplies are sent when a patient is randomised, but may be used for any patient within the study please specify.

Indicate if a QP release is required and whether this will be in advance or with delivery or should be requested after delivery and from whom. State by which means this will occur (i.e. Fax, email, phone etc).

Specify any arrangements on receipt of supplies such as faxing an 'Acknowledgment of Receipt Form' or logging the receipt with an Interactive Voice Response System (IVRS) / Interactive Web Response System (IWRS).

Indicate what should be done if supplies are damaged on arrival.

State whether sites will be notified by fax/email of any impending delivery.

<sup>3</sup> If there is reimbursement of hospital stocks please state whether this is in money or free drug and give details of the reimbursement procedure.

<sup>4</sup> "Buy one get one free" type of discounts should be avoided: A 50% discount is preferable

<sup>5</sup> All cytotoxic tablets/capsules should be provided in blister strips

## **4. Randomisation**

### **4.1. Process**

Give details of the randomisation procedure.  
State who will receive new patient/randomisation alerts e.g. investigator/research nurse/pharmacy.  
State how they will be sent e.g. fax/email.

### **4.2. Code breaks**

If the trial is double-blinded give details of who holds the code-breaks and the procedure for unblinding.  
If an automated IVRS/IWRS system is used give details of who will have access to the unblinding facility e.g. investigator/pharmacy.

## **5. Prescribing**

State whether a trial specific prescription has been designed for use in the trial. If provided, must the prescription be used as it is or may it be modified? Can centres use their own prescriptions as alternative? This may include those generated by electronic prescribing systems.  
State whether dose banding is permitted according to local policy and for which medicines.  
State whether dose capping is mandatory and specify the cap.  
State whether actual or ideal body weight should be used in calculations.  
State method of calculating body surface area (BSA) and whether BSA/doses should be recalculated at each cycle or only under certain circumstances,  
State formula for carboplatin dosing.  
State whether rescue medications are permitted and give details.

## **6. Dispensing**

State the procedure and amounts to be given on each occasion. In the case of orally administered IMP, consider whether this is compatible with the pack size supplied, thereby allowing the pharmacy department to maintain Annex 13 compliant labeling.  
Describe the dosage form, packaging and labeling of IMP and additional arrangements for labeling blinded drug supplies.  
Indicate if any written material is to be given to the patient, for example capecitabine diary, diary for the use of rescue medicines, instructions on how to use or take medicines.  
State whether any additional supplementary/warning labels are required.

## **7. Accountability forms**

Give details of documentation required and for which drugs. For drug accountability/ dispensing logs, state whether they are patient specific or batch specific etc.  
State any requirements such as faxing/sending copies to the trial co-ordinating centre on completion.  
List documentation provided and state whether hospitals are allowed to use their own documentation if preferred.  
If end-of-study drug reconciliation is required, please state this.  
Appropriate forms should be provided (see section 9).

Clearly distinguish between a) 'full drug accountability' and b) 'drug accountability/traceability'

- a) 'Full drug accountability' i.e. accounting for all IMPs provided to a site. (What has come in to a site, what has gone out to which patients, what has been destroyed/returned to sponsor, what is left on the shelf). In the event of a drug recall can all patients who received any of the affected batch be identified. This requires drug accountability/dispensing logs;
- b) 'Drug accountability/traceability' e.g. for IMP/NIMP from hospital stocks. (What has gone out to which patients)? In the event of a drug recall can all patients who received any of the affected batch be identified. This information could be captured on pharmacy aseptic unit worksheets or drug accountability/dispensing logs

## 8. Patient returns

State which drug(s)<sup>6</sup>, if any, are expected to be returned from the patient to the hospital/site/pharmacy.

State what is required to be done with the returns (and by whom); count and record in the CRF or in the pharmacy documentation, save the returns until verified by a monitor or dispose of as convenient, return to the sponsor/supplier or destroy on site.

## 9. Destruction

Give details of the disposal of used drug, partially used drug, drug left unused at the end of the study and expired drug.

Disposal may be by either returning drugs to the sponsor/supplier or by disposal at site.

If the co-ordinating centre would like a copy of any certificates of disposal, state this and how to send the copy (fax, post). If the co-ordinating centre would like to give authorisation before any disposal please state this. If off site external contractor is used for disposal no certificate for destruction can be obtained.

## 10. Hazards

State any specific requirements associated with study drugs (IMP/NIMP's) in regard to spillages on surfaces and on personnel handling product.

## 11. Forms/Templates

The following forms/templates should be included as appendices where applicable. State how each should be completed and by whom:

- Patient log
- Accountability logs – see sample logs in Appendix 1 (per drug) and Appendix 2 (per patient)
- Destruction form for IMPs
- Trial specific order form for IMPs
- Prescription
- Temperature log
- Pharmacy personnel log
- Delegation log
- CV template

<sup>6</sup> For health and safety reasons used and partially used vials of cytotoxics/monoclonal antibodies are not kept (and neither are the outer boxes).

**Appendix 1**

**Sample accountability log (per drug)**

<Identifier, e.g. Trial Name/Acronym>

Master <Drug/Device> Accountability Log

Site:

Principal Investigator:

| Date                            | Action  | <Drug strength 1> |                 |                | To be completed for dispensed items |              |      |         | Please complete this section for all actions |                       |          |                 |           |          |
|---------------------------------|---|-------------------|-----------------|----------------|-------------------------------------|--------------|------|---------|--|-----------------------|----------|-----------------|-----------|----------|
|                                 |   | Quantity          | Batch Number(s) | Expiry Date(s) | Patient's Initials                  | Trial Number | Dose | Balance | Dispensed/Received by (initials)             | Checked by (initials) | Returned |                 | Destroyed |          |
|                                 |   |                   |                 |                |                                     |              |      |         |  |                       | Quantity | Initials + Date | Date      | Initials |
|                                 | <input type="checkbox"/> Receipt<br><input type="checkbox"/> Dispensing |                   |                 |                |                                     |              |      |         |  |                       |          |                 |           |          |
|                                 | <input type="checkbox"/> Receipt<br><input type="checkbox"/> Dispensing |                   |                 |                |                                     |              |      |         |  |                       |          |                 |           |          |
|                                 | <input type="checkbox"/> Receipt<br><input type="checkbox"/> Dispensing |                   |                 |                |                                     |              |      |         |  |                       |          |                 |           |          |
|                                 | <input type="checkbox"/> Receipt<br><input type="checkbox"/> Dispensing |                   |                 |                |                                     |              |      |         |  |                       |          |                 |           |          |
|                                 | <input type="checkbox"/> Receipt<br><input type="checkbox"/> Dispensing |                   |                 |                |                                     |              |      |         |  |                       |          |                 |           |          |
|                                 | <input type="checkbox"/> Receipt<br><input type="checkbox"/> Dispensing |                   |                 |                |                                     |              |      |         |  |                       |          |                 |           |          |
|                                 | <input type="checkbox"/> Receipt<br><input type="checkbox"/> Dispensing |                   |                 |                |                                     |              |      |         |  |                       |          |                 |           |          |
|                                 | <input type="checkbox"/> Receipt<br><input type="checkbox"/> Dispensing |                   |                 |                |                                     |              |      |         |  |                       |          |                 |           |          |
|                                 | <input type="checkbox"/> Receipt<br><input type="checkbox"/> Dispensing |                   |                 |                |                                     |              |      |         |  |                       |          |                 |           |          |
|                                 | <input type="checkbox"/> Receipt<br><input type="checkbox"/> Dispensing |                   |                 |                |                                     |              |      |         |  |                       |          |                 |           |          |
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## **Appendix 2**

### **Sample accountability log (per patient)**

<Identifier, e.g. Trial Name/Acronym>

**Patient Specific <Drug/Device> Accountability Log**

**Site:**

**Trial number:**

**Principal Investigator:**

**Patient initials:**

| <b>&lt;Drug/Device&gt; &lt;units&gt;</b> |   |              |             |                 |                        |                       |   |                                  |                 |                            |                  |                 |
|--|---|--------------|-------------|-----------------|------------------------|-----------------------|---|----------------------------------|-----------------|----------------------------|------------------|-----------------|
| <b>Date</b>                              | <b>Action</b>   | <b>Cycle</b> | <b>Dose</b> | <b>Quantity</b> | <b>Batch Number(s)</b> | <b>Expiry Date(s)</b> | <b>Dispensed /<br/>Received by<br/>(initials)</b> | <b>Checked by<br/>(initials)</b> | <b>Returned</b> |                            | <b>Destroyed</b> |                 |
|  |   |              |             |                 |                        |                       |   |                                  | <b>Quantity</b> | <b>Initials<br/>+ Date</b> | <b>Date</b>      | <b>Initials</b> |
|  | <input type="checkbox"/> Receipt<br><input type="checkbox"/> Dispensing |              |             |                 |                        |                       |   |                                  |                 |                            |                  |                 |
|  | <input type="checkbox"/> Receipt<br><input type="checkbox"/> Dispensing |              |             |                 |                        |                       |   |                                  |                 |                            |                  |                 |
|  | <input type="checkbox"/> Receipt<br><input type="checkbox"/> Dispensing |              |             |                 |                        |                       |   |                                  |                 |                            |                  |                 |
|  | <input type="checkbox"/> Receipt<br><input type="checkbox"/> Dispensing |              |             |                 |                        |                       |   |                                  |                 |                            |                  |                 |
|  | <input type="checkbox"/> Receipt<br><input type="checkbox"/> Dispensing |              |             |                 |                        |                       |   |                                  |                 |                            |                  |                 |
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|  | <input type="checkbox"/> Receipt<br><input type="checkbox"/> Dispensing |              |             |                 |                        |                       |   |                                  |                 |                            |                  |                 |
|  | <input type="checkbox"/> Receipt<br><input type="checkbox"/> Dispensing |              |             |                 |                        |                       |   |                                  |                 |                            |                  |                 |

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