The Global Health Network

Sourcing, Preparing and Accounting for Investigational Products

Nicky Kramer and Wynand Smythe
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actually...
IMP (Investigational Medicinal Product) / IP (Investigational Product)

1. Sourcing and Receipt
2. Storage
3. Dispensing/Blinding
4. Randomisation
5. Disposal/Destruction
IMP/IP

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1. Sourcing and Receipt
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Sourcing and Receipt

**Sponsor-driven Phase I:**
- New IMP & Formulation
- Sponsor arranges manufacture
- Importing
- Dummy Dispensing

**Investigator-led Phase III:**
- Typically Locally-Marketed Product
- Pharmacist sources IMP
- Dummy Dispensing

**Source of Accountability:**
Delivery waybills, Prescriptions, Invoices, Receipt Accountability
## Receipt Accountability

**Sourcing and Receipt**

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### Source of Accountability:
- Delivery waybills,
- Prescriptions,
- Invoices,
- Receipt

### IMP receipt form

<table>
<thead>
<tr>
<th>Item</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>Name of IP (if applicable)</td>
<td></td>
</tr>
<tr>
<td>Dosage form</td>
<td></td>
</tr>
<tr>
<td>Packaging form</td>
<td></td>
</tr>
<tr>
<td>Manufacturer</td>
<td></td>
</tr>
<tr>
<td>Lot/batch no.</td>
<td></td>
</tr>
<tr>
<td>Expiry date</td>
<td></td>
</tr>
<tr>
<td>Date of manufacture</td>
<td></td>
</tr>
<tr>
<td>Date of receipt</td>
<td></td>
</tr>
<tr>
<td>Received from</td>
<td></td>
</tr>
<tr>
<td>Storage conditions</td>
<td></td>
</tr>
<tr>
<td>Type of documentation received</td>
<td></td>
</tr>
</tbody>
</table>
IMP (Investigational Medicinal Product) / IP (Investigational Product)

1. Sourcing and Receipt
2. Storage
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4. Randomisation
5. Disposal/Destruction
Storage

- Certificate of Analysis (COA)
  - light, temperature, humidity

- Rigorous Control
  - E.g. fridges, air-con, probes, light protection

- Unique Storage Space

- Back-Up Plan

Sources of Accountability:
Temperature Logs, Calibration Certificates, SOPs, COAs
IMP (Investigational Medicinal Product) / IP (Investigational Product)

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Dispensing

- Dispensing Licence
- Expiry Dates
- IP prep (e.g. reconstitution, infusion)
- Labelling requirements
  - e.g. Participant ID, Study/Protocol/Investigator ID, Quantity Dispensed, Mode of Delivery, Storage Condition, Exp./Lot/Batch #’s
- Blinding - implication for dispensing directly to patient
- Unblinding procedure

Source of accountability:
MCC documentation, Pharmacy Manual (accountability, labels, patient dispensing logs)
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**Source of Accountability:**
- Delivery waybills,
- Prescriptions,
- Invoices,
- Receipt Accountability

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**Pharmacy/IMP store accountability form**

**Protocol number/title:**

**IMP name/formulation:**

**Investigator (indicate PI, National, coordinating):**

**Batch/lot number and expiry date:**

### IMP RECEIVED at Pharmacy/IMP Store

<table>
<thead>
<tr>
<th>DATE</th>
<th>IMP RECEIVED at Pharmacy/IMP Store</th>
<th>IMP removed from Pharmacy/IMP Store</th>
<th>Balance</th>
<th>Signature/date of pharmacist</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Transaction:</td>
<td>Transaction:</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Shipment from supplier</td>
<td>• Return to supplier</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Return from site / ward</td>
<td>• Supply to site / ward</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Packing / labelling</td>
<td>• For destruction</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Participant numbers</td>
<td>Participant numbers</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>No. of [units]</td>
<td>No. of [units]</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Packed</td>
<td>Packed</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Unused</td>
<td>Unused</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Unpacked</td>
<td>Unpacked</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Comments:

**PI signature:**

**Date**
IMP/IP

IMP (Investigational Medicinal Product) / IP (Investigational Product)

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Randomisation

- Treatment Allocation/Dispensing
  - Generated by statistician/pharmacist (sponsor or site produced), stored in secure location e.g. pharmacy file
    - Randomisation schedule or Automated system e.g. IVRS

- Randomisation log

Source of accountability: Randomisation schedule and Randomisation logs
### Sourcing and Receipt

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**Source of Accountability:**
- Delivery waybills
- Prescriptions
- Invoices

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**Randomisation Schedule Accountability**

<table>
<thead>
<tr>
<th>Study number</th>
<th>University of Cape Town Clinical Research Centre</th>
<th>Sponsor</th>
<th>Acknowledgement of IP receipt</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Randomization list for Somerset Hospital</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Enrolment number</th>
<th>Treatment allocation</th>
<th>Signature</th>
<th>Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Screening01</td>
<td>Placebo</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Screening02</td>
<td>Active</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Screening03</td>
<td>Active</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Screening04</td>
<td>Placebo</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Screening05</td>
<td>Active</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Screening06</td>
<td>Placebo</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Screening07</td>
<td>Active</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Screening08</td>
<td>Placebo</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
# Randomisation Log Accountability

## Randomization Log for: **ACTIVE IMP**

<table>
<thead>
<tr>
<th>Step</th>
<th>Check</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>IMP with “non-blinded” treatment label</td>
<td></td>
<td>Batch n°_________</td>
</tr>
<tr>
<td>Apply the final “blinded” treatment label with the subject randomization number and complete all fields</td>
<td></td>
<td>Study code-enrolment #</td>
</tr>
<tr>
<td>Remove the original “non-blinded” treatment label and stick it here</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Randomization by:**

<table>
<thead>
<tr>
<th>Name</th>
<th>Name</th>
</tr>
</thead>
</table>

**Randomization controlled by:**

<table>
<thead>
<tr>
<th>Name</th>
<th>Name</th>
</tr>
</thead>
</table>

## Randomization Log for: **PLACEBO FOR IMP**

<table>
<thead>
<tr>
<th>Step</th>
<th>Check</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>IMP with “non-blinded” treatment label</td>
<td></td>
<td>Batch n°_________</td>
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Return/disposal

- At conclusion of study, final inventory and reconciliation
- Sponsor-driven: return to sponsor for disposal or site arranges disposal
- Arrange with waste disposal company

Source of accountability: Disposal/Destruction Log
**Sourcing and Receipt**

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**Source of Accountability:**
- Delivery waybills
- Prescriptions
- Invoices

**Destruction Log Accountability**

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**IMP receipt for destruction form**

<table>
<thead>
<tr>
<th>Protocol number/title:</th>
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</thead>
</table>

<table>
<thead>
<tr>
<th>Investigator (indicate PI, National, coordinating):</th>
</tr>
</thead>
</table>

This is to certify the delivery of the clinical trial pharmaceutical listed below to a drug disposal organisation.

<table>
<thead>
<tr>
<th>IMP name/number</th>
<th>Formulation</th>
<th>Quantity</th>
<th>Batch/lot no</th>
<th>Expiry date</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Packed</td>
<td>Unpacked</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Used</td>
<td>Unused</td>
<td></td>
</tr>
</tbody>
</table>

**Authorised by**

<table>
<thead>
<tr>
<th>Designation</th>
<th>Signature</th>
<th>Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Principal Investigator</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Delivered by**

<table>
<thead>
<tr>
<th>Designation</th>
<th>Signature</th>
<th>Date</th>
</tr>
</thead>
</table>
SUMMARY

• Importance of pharmacy role: **maintains accountability of IMP from start to finish, ensuring right dose given to right patient at the right time**

• Accountability is a continuous process from start of study until closure

• Inform/involve pharmacy at the outset

• Resources available on CRC website - [http://www.crc.uct.ac.za/](http://www.crc.uct.ac.za/)
SUMMARY

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Investigational products

Medicines

South African GCP has the following definition for an Investigational Product (which is synonymous with Study Product, and termed Investigational Medicinal Product (IMP) in Europe):

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.

Trials using Investigational Products must adhere to South African Good Clinical Practice (GCP) and Good Pharmacy Practice (GPP), both of which reference South African Good Manufacturing Practice (GMP).

If the Investigational Product is not pre-packaged by the Sponsor, and uses anything other than a simple dilution or reconstitution, please talk to the CRC for advice about whether you must adhere with the onerous full GMP requirements.

Whoever compounds and/or dispenses Investigational Product must be legally authorized to do. Currently this situation is unclear, however, it appears to be that, for clinical trials, a registered nurse is not allowed to dispense.

Devices

Toolkit

SOPs
Receiving IMP
Packaging and labeling IMP
Dispensing, dosing and return of IMP
Disposal of IMP

IMP receipt form
Pharmacy IMP store accountability form
Label requisition and printing form
IMP label
Packing of IMP form
Investigator accountability form
IMP return form
IMP receipt for destruction form

Factsheets
Destruction of IMP
Importing study drugs

Other useful documents
Questions?