The role of Pharmacy in Clinical Trials

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Overview

• Roles of pharmacy in cancer research
• Pharmacy specific issues to consider when sponsoring or hosting a CTIMP
Why is pharmacy needed?

- Legal requirement to handle IMPs within UK, EU and international legislation
- IMP management delegated from CI/PI to named trials pharmacist
- All IMP trials will come through pharmacy – important to understand pharmacy processes.
GCP in relation to Pharmacy?

‘Investigational products should be manufactured, handled, and stored' in accordance with applicable GMP. They should be used in accordance with the approved protocol’

‘A trial should be conducted in compliance with the protocol that has received prior institutional review board/independent ethics committee approval/favourable opinion’

‘Each individual involved in conducting a trial should be qualified by education, training, and experience to perform his or her respective task(s).’

‘The confidentiality of records that could identify subjects should be protected, respecting the privacy and confidentiality rules in accordance with the applicable regulatory requirement(s).’

‘Systems with procedures that assure the quality of every aspect of the trial should be implemented’

GCP
Assessing capacity and capability for research
Feasibility Review – what are we looking for?

- Best practice - All IMP trials should be assessed by Pharmacy before sites open to recruitment
- Do we have capacity?
  - Treatment complexity & frequency of dose preparation and dispensing
  - Number of expected patients
  - Expected trial duration
  - Complexity of dispensing & aseptic manipulation
  - Staff requirements
  - Drug (excess treatment costs) or equipment costs
Feasibility Review – what are we looking for?

Legally

• Is it manufacture vs hospital exemption? Is an IMP license required?
• Are we receiving drug for another site and sending it on? Is a wholesaler’s license required?
• Is IMP being shipped directly to Trust from outside EU? Do we need a import license?
Feasibility Review – what are we looking for?

Technical

• Novel agent vs licensed product,
• Storage requirements (e.g. -80°C +/- 10 °C)
• Aseptic or ward preparation?
• Stability e.g. From point of dilution to end of infusion 4 hr expiry and 1hr infusion, can get to patient in time?
• Additional equipment required e.g sonicator for gene therapy trial, sourcing of infusion bags, giving sets etc
Contracts and Costings

• Commercial Studies:
  – Provide pharmacy fees for set-up, dispensing of IMP and trial maintenance
  – Negotiate fees with commercial sponsors and liaise with contracts manager and trial coordinators
  – Review any pharmacy specific clauses e.g. pharmacy appendix to contract.

• Non-Commercial Studies:
  – Review clauses in contracts around IMP management.
  – Negotiate fees where possible
Trial Set Up

• Prepare trial related procedures and prescriptions

• Liaise with Sponsor to clarify details
  – Packaging
  – Labelling
  – Diluents/giving set etc.
  – IVRS access and process
  – Drug supply – ordering etc.
Additional Trial requirements

• Annex 13 of EU GMP:
  – Sponsor details
  – PI
  – ‘For Clinical Trial Use Only’
  – Batch number and Expiry
  – Site number
  – Patient number
IMP Storage

Do IMPs have special storage requirements?
Once we are open…
Pharmacy

- At RMH trial prescriptions may pass through 8 different members of the pharmacy team
  - Screener (pharmacist)
  - Dispenser (ATO or technician)
  - Checker (senior technician or pharmacist)
  - For Aseptically prepared products –
    - Worksheet preparation (technician)
    - Tray preparation (ATO or technician)
    - Preparation of final product (technician)
    - Bagging up and labelling of final product (ATO or technician)
    - Final check and release (senior technician or pharmacist)
Clinical Screen of Trial Rx

• Always done by a pharmacist
• Involves checking:
  – Correct drugs
  – Appropriate duration + frequency of treatment
  – Appropriate doses (e.g. for age, weight, BSA)
  – Appropriate administration (i.e. route, rate, diluent)
  – Prescribed legally (e.g. controlled drug prescriptions)
  – Any potential interactions between medications
  
  – What monitoring is necessary to ensure patient safety?

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… Clinical Screen of Trial Rx

- Blood results - Is it safe for patient to received cytotoxics?
  - FBC: Hb>10, Plts>100x10^9/L, Neuts>1x10^9/L
  - Renal function (serum Creatinine, CrCl)
  - Liver function (ALT/AST, Bilirubin, GGT)
  - Other parameters e.g. Albumin for ifosfamide

- Dose delays or reductions per protocol?
  Guided by grade toxicity in line with CTCAE
Dispensing/Checking

• Not just ‘counting pills’
• UK labelling requirements –
  – Patient name
  – Drug name, strength, form
  – Directions for use
  – Keep out of the reach and sight of children
  – Date of dispensing
  – Name and address of person supplying medicinal product
  – Any cautionary labels (e.g. take one hour before food, avoid antacids while taking this medication)
Dispensing/Checking

• Checking against the prescription:
  – Correct patient details
  – Correct drug, strength, formulation, quantity
  – Correct dose + administration instructions
• Correct labelling
• Correct accountability documented
• Expiry covers total intended treatment period
Aseptic Preparation of Products

- Aseptic unit – controlled set of rooms to minimise risk of microbial contamination of medicinal products
IMPORTANT
STORE BETWEEN
+2°C AND +8°C
ON RECEIPT

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# Trial Prescriptions

**Trial Number:** BRIM-3  
**CCR:** 3.362  
**PN:** NO25026-EU  
**Arm B:** Dacarbazine

**Cycle:** (repeat every 3 weeks)

<table>
<thead>
<tr>
<th>Date</th>
<th>Hb</th>
<th>WBC</th>
<th>Neut</th>
<th>PLT</th>
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<tbody>
<tr>
<td></td>
<td>g/dL</td>
<td>x 10^9/L</td>
<td>x 10^9/L</td>
<td>x 10^9/L</td>
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<table>
<thead>
<tr>
<th>Urea</th>
<th>Cr</th>
<th>ALT</th>
<th>Bilirubin</th>
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<tbody>
<tr>
<td>mmol/L</td>
<td>µmol/L</td>
<td>µL</td>
<td>µmol/L</td>
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<table>
<thead>
<tr>
<th>Admin Date</th>
<th>Admin time</th>
<th>Drug</th>
<th>Dose</th>
<th>Route</th>
<th>Infusion duration</th>
<th>Administration details</th>
<th>Prescriber Signature</th>
<th>Date</th>
<th>Time</th>
<th>Signature</th>
</tr>
</thead>
<tbody>
<tr>
<td>T-10min</td>
<td></td>
<td>Dexamethasone</td>
<td>8mg</td>
<td>IV</td>
<td>bolus</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>T-10min</td>
<td></td>
<td>Chloroquine (10mg if &gt;100kg)</td>
<td>8mg</td>
<td>IV</td>
<td>bolus</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Day 1</td>
<td>T=0</td>
<td>Dacarbazine 1000mg/m²</td>
<td>mg</td>
<td>IV</td>
<td>1 hour</td>
<td>In 1000ml Sodium chloride 0.9%</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>TTOs</strong></td>
<td></td>
<td>Dexamethasone</td>
<td>4mg</td>
<td>po</td>
<td>tds</td>
<td>For 3 days</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Metoclopramide</td>
<td>10mg</td>
<td>po</td>
<td>tds</td>
<td>For 3 days then pm</td>
<td></td>
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</tbody>
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Patient authorised to receive above medication by:

**Signature of Pharmacist:**

**Drs Signature:** __________________________ Date: ____________  
**Date:** ____________
Conclusion

• Lots of legislation and plenty to do!
• Obtaining pharmacy input when designing CTIMPs should reduce set up time, the number of queries/problems.