Pharmacists’ involvement in clinical trials and ethical committees

“Rene Grouls - Conflict of interest: nothing to disclose”.

The role of the pharmacy in clinical research is:

- To safeguard subjects, health care professionals and the Healthcare Provider Organisation (HPO) by ensuring that IMPs are appropriate for use and are procured, handled, stored and used safely and correctly.
- To ensure that IMPs are managed and dispensed to patients in accordance with the duly approved current protocol.
- To ensure that all pharmacy clinical trials procedures comply with relevant guidelines and regulations.
Pharmacists’ involvement in clinical trials and ethical committees

Trial Development Phase

Needed:

- GMP production facilities
- GMP approved quality system
- GMP trained personnel
- Manufacturing authorisation
- Knowledge
  - GMP, GCP, GLP etc.
  - Product development
  - IMPD development
  - Etc
  = TEAMWORK
Pharmacists’ involvement in clinical trials and ethical committees

Trial Development Phase - IMPD

Clinical Trials Directive (2001/20/EC)

The IMPD includes summaries of information related to the quality, manufacture and control of the Investigational Medicinal Product, data from non-clinical studies and from its clinical use. An overall risk-benefit assessment, critical analyses of the non-clinical and clinical data in relation to the potential risks and benefits of the proposed study have to be part of the IMPD.

Pharmacists’ involvement in clinical trials and ethical committees

Trial Development Phase

In the Netherlands:

14
Pharmacists’ involvement in clinical trials and ethical committees

MREC Review Phase

In Dutch:

competent authority for the (marginal) review of research with a medicinal product.

The decentral review lies in the hands of the accredited medical ethical research committees (MRECs).

<table>
<thead>
<tr>
<th>Role</th>
<th>Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hospital pharmacist</td>
<td>14</td>
</tr>
<tr>
<td>Hospital pharmacist/clinical pharmacist</td>
<td>43</td>
</tr>
<tr>
<td>Hospital pharmacist/clinical toxicologist</td>
<td>1</td>
</tr>
<tr>
<td>Chairman</td>
<td>4</td>
</tr>
<tr>
<td>Vice-chairman</td>
<td>1</td>
</tr>
<tr>
<td>Clinical pharmacologist</td>
<td>3</td>
</tr>
<tr>
<td>Methodologist</td>
<td>1</td>
</tr>
</tbody>
</table>
Pharmacists’ involvement in clinical trials and ethical committees
MREC Review Phase

<table>
<thead>
<tr>
<th>24 accredited MRECs</th>
<th>CLINICAL PHARMACOLOGIST</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hospital pharmacist</td>
<td>• Be registered as a clinical pharmacologists by the Dutch Society of Clinical Pharmacology and Biopharmacy;</td>
</tr>
<tr>
<td>Hospital pharmacist/clinical pharmacologist</td>
<td>• Have demonstrable experience with clinical pharmacological research (experimental and/or observational drugs trials involving human subjects), shown from publications and/or dissertation;</td>
</tr>
<tr>
<td>Hospital pharmacist/clinical toxicologist</td>
<td>• Have at least three years experience working in the field of clinical pharmacology within the five years preceding application for recognition as an MREC member</td>
</tr>
<tr>
<td>Chairman</td>
<td></td>
</tr>
<tr>
<td>Vice-chairman</td>
<td></td>
</tr>
<tr>
<td>Clinical pharmacologist</td>
<td></td>
</tr>
<tr>
<td>Methodologist</td>
<td></td>
</tr>
</tbody>
</table>

Pharmacists’ involvement in clinical trials and ethical committees
MREC Review Phase

WMA Declaration of Helsinki - Ethical Principles for Medical Research Involving Human Subjects

Operational Guidelines for Ethics Committees That Review Biomedical Research
Pharmacists’ involvement in clinical trials and ethical committees
MREC Review Phase

- Why is the study being done?
- What happens if I change my mind after I enroll in the study?
- What treatment options do I have for my condition?
- What are the advantages of participating in this trial?
- What are the disadvantages of trial participation?
- What are the results of earlier studies on this treatment?
- What kinds and how often will tests be performed?
- Who will pay for these tests and treatments?
- Who will my doctor be?
- Will there be travel involved?
- Who pays for travel expenses?
- Will participation affect my daily life?
- What side effects might I expect?
- Will this require hospitalization?
- How long will the study last?
- What type of long-term follow-up will there be?
- Can treatment continue past the end of the study?
- Any other participants that I can speak to?
- If harmed by the research, what treatment am I entitled to?
Pharmacists’ involvement in clinical trials and ethical committees
MREC Review Phase IMPD

**IMPD CHECKLIST**

- IMP supply agreement(s) with contract manufacturer(s) and amendments
- Technical agreement(s) with contract manufacturer(s)

**Clinical Trial IMP Documentation**
- The CTA and any subsequent amendments
- The MRA acceptance letter
- Final letter from Research Ethics Committee
- Summary of drug arrangements
- Product Information (Full/Simplified IMPD)
- IMP safety information document (IB or SPC)
- IMP licence list in the national language
- MA (IMP) licence of final QP releasing site
- MA (IMP) licence of placebo manufacturing site + Certified QP release statement
- Import QP release certificate (if applicable)
- QP declaration
- IMP certificate of analysis
- Viral safety studies and data (if applicable)
- TSE-free certificate(s)
- Master randomisation list
- IMP prescription template
- IMP accountability log template
- IMP destruction log template
- Temperature log template (if not using site documentation)
- Temperature deviation log template
- IMP recall information
- IMP code breaks

Clinical Trials Toolkit: Trial Supplies 2012 (MODEPHARMA)

**IMPD Case**

- Comparison: IMAGINOMAB 100 vs Placebo
- Pharmacy technician: unblinded
- Administration: blinded
- Injection Scheme:
  - 1 IMAGINOMAB 100 + 1 Placebo
  - 2 IMAGINOMAB 100
  - 2 Placebo

Pharmacists’ involvement in clinical trials and ethical committees
IMPD Case

![Image](image.jpg)
Pharmacists’ involvement in clinical trials and ethical committees
Ethics - Time to decide – Informed Consent

New aortic valve and valve delivery system

Objectives:
• Cardiac performance
• Adverse events

Regular “planned” intervention

Time to Decide

• General Assessment and Registration (Dutch: ABR) form: “As Long as Needed”
• Patient Information: “Not mentioned”
• Physician: “We ask them day before or the day of intervention”
• MREC: “At least 1 week”

LESSON: ALWAYS CONCRETE TIME FRAMES

Pharmacists’ involvement in clinical trials and ethical committees
Ethics - Time to decide – Informed Consent

11 pages
Pharmacists’ involvement in clinical trials and ethical committees

SUSARs and Development Safety Update Reports (DSURs)

The DSUR should include:

- Analysis of the subjects’ safety in the concerned clinical trial(s) with an appraisal of its ongoing risk:benefit
- A line listing of all suspected serious adverse reactions (including all SUSARs) that occurred in the concerned trial(s), including all serious adverse reactions from third countries
- An aggregate summary tabulation of suspected serious adverse reactions that occurred in the concerned trial(s).

Pharmacists’ involvement in clinical trials and ethical committees

MREC Review Phase

Needed:

- Knowledge
  - GMP, GCP, GLP etc.
  - Product development
  - IMPD
  - Etc
  = TEAMWORK
- Critical Attitude
- Time
Pharmacists’ involvement in clinical trials and ethical committees
Trial Implementation Phase – An Historical Anecdote (n=1)

2 Decades ago

- Trials without Pharmacy Intervention
- 10 trials
- 840 pts included
- 8% drop-outs caused by incomplete documentation
- 5.6% drug accountability related

2 Years later

- All Trials with IMP with Pharmacy Intervention
- 8 trials
- 536 pts included
- 2% drop-outs caused by incomplete documentation
- <1% drug accountability related

Pharmacists’ involvement in clinical trials and ethical committees
Trial Implementation Phase

Needed:

- GMP/GCP facilities
- GCP approved quality system
- GMP/GCP trained personnel
- Knowledge
  - GMP, GCP, GLP etc.
  = TEAMWORK
Pharmacists’ involvement in clinical trials and ethical committees

Trial Implementation Phase

Staff

- Hospital Pharmacist
- Hospital Pharmacist in training
- 3 Pharmacy Practitioners

All other Hospital Pharmacists/Pharmacy Practitioners

Approx. 200 on-going trials

Standard operating procedures (SOPs)

- Pharmacy approval of a clinical trial
- Receipt/recording of the safe delivery of IMPs
- Safe handling and storage of IMPs
- Temperature monitoring and reporting of temperature deviations
- Risk assessment of storage areas for IMPs outside pharmacy
- Preparation and dispensing of IMPs in accordance with professional standards
- Return and disposal of unused IMPs
- Reconciliation of IMPs
- Drug alerts and recalls of IMPs
- Maintaining a pharmacy study file
- Training of clinical trial pharmacy staff
- Archiving of clinical trials documentation
- Quarantine of IMPs
- Expiry date relabelling
- Unblinding

What you get in return:

- Cooperation with physicians etc..
- Knowledge
- Cooperation with MREC members
- Frontline of new developments
Pharmacists’ involvement in clinical trials and ethical committees

Thank You