Pharmacists' involvement in clinical trials and ethical committees

Focus on The Netherlands

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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

Professional Guidance on Pharmacy Services for Clinical Trials, Version 1, October 2013, Royal Pharmaceutical Society of Great Britain

OBJECTIVES

The primary aim of a pharmacy investigational drugs service is to optimise quality use of investigational drugs. The specific objectives are to:

- support and promote the safe and ethical use of investigational drugs;
- apply the principles of best pharmacy practice to the evaluation of new drugs;[5]
- ensure pharmacy aspects of investigational drug use comply with relevant legislative acts, standards and guidelines;
- consider the safety and welfare of participants and protection of their rights, confidentiality and privacy; and
- support and promote clinical and pharmacy research.

SHPA Standards of Practice for Pharmacy Investigational Drugs Services. J Pharm Pract Res 2006; 36 (1) 46-53

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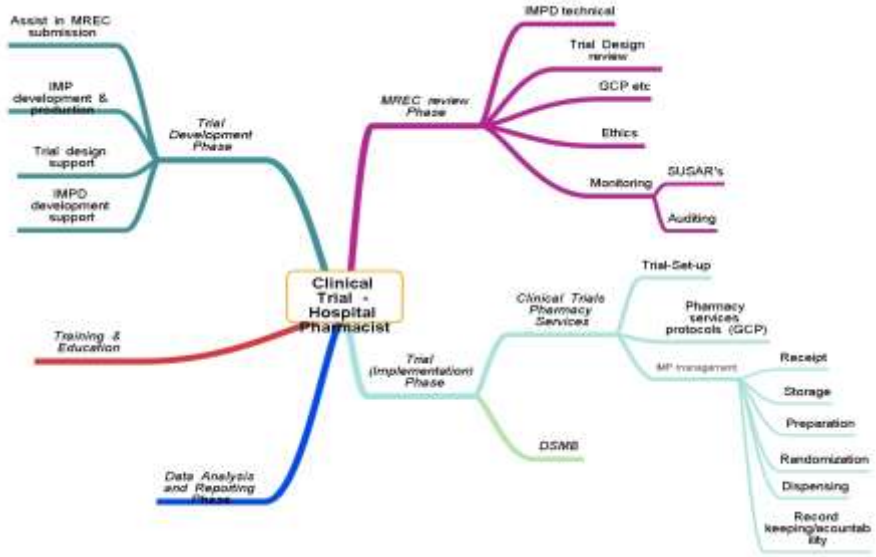
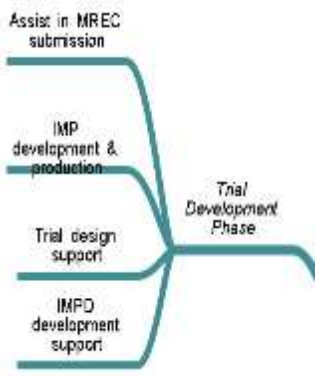


Pharmacists' involvement in clinical trials and ethical committees
Trial Development Phase



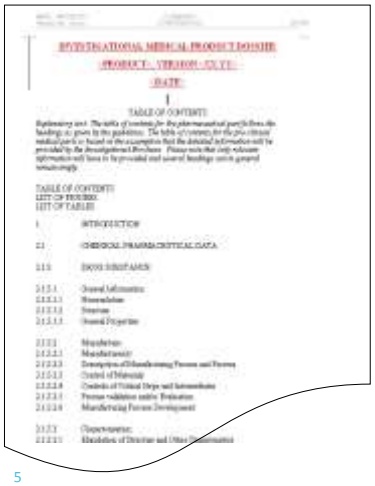
Needed:

- GMP production facilities
- GMP approved quality system
- GMP trained personnel
- manufacturing authorisation
- Knowledge
  - GMP, GCP, GLP etc.
  - Product development
  - IMPD development
  - Etc

  = TEAMWORK

4

Pharmacists' involvement in clinical trials and ethical committees
Trial Development Phase - IMPD



5

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.

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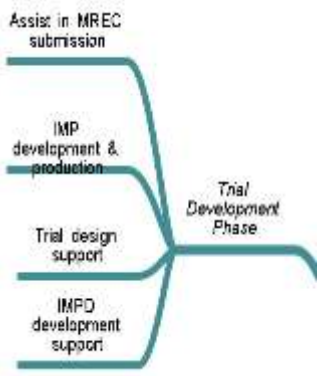
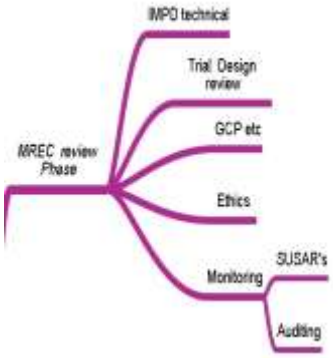
Trial Development Phase



In the Netherlands:

6

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



In Dutch:

ccmo

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).

7

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

24 accredited MRECs	
Hospital pharmacist	14
Hospital pharmacist/clinical pharmacologist	43
Hospital pharmacist/clinical toxicologist	1
Chairman	4
Vice-chairman	1
Clinical pharmacologist	3
Methodologist	1

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

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CLINICAL PHARMACOLOGIST

- Be registered as a clinical pharmacologists by the Dutch Society of Clinical Pharmacology and Biopharmacy;
- Have demonstrable experience with clinical pharmacological research (experimental and/or observational drugs trials involving human subjects), shown from publications and/or dissertation;
- 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

9

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MREC Review Phase

10

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MREC Review Phase

ETHICS ARE LOCAL: ENGAGING CROSS-CULTURAL VARIATION IN THE ETHICS FOR CLINICAL RESEARCH

11

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MREC Review Phase In General – USE CHECKLISTS

- ❑ 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?

12

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MREC Review Phase IMPD

IMPD CHECKLIST

Agreements

- ❑ 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 MHRA 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 label texts 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)

13

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IMPD Case

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

14

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

15

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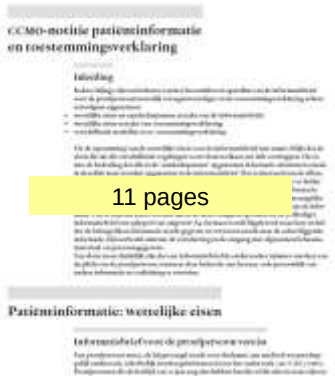
Ethics - Time to decide – Informed Consent


CCMO-notitie patiëntinformatie en toestemmingsverklaring

Inleiding

11 pages

Patiëntinformatie: wettelijke eisen

What do our patients understand about their trial participation? Assessing patients' understanding of their informed consent consultation about randomised clinical trials

C Behrendt,[1] T Gibb,[2] C Roeske,[3] H Bertz,[2] A Wünsch[1]

(1) Recall of information about IC; (2) recall of content; (3) recall of RCT process

The 10 interviews show a low recall of information about the clinical trial by the patients. One patient stated: *"I only wanted to sleep and he basically made my ears bleed. I didn't understand anything"*.

Some patients knew about the concept of RCTs but certain indifference was detected as clarified in this patient's citation: *"They might have sold me 20 washing machines and I would have signed it. I would have signed anything at that moment"*.

J Med Ethics 2011;37:74–80. doi:10.1136/jme.2010.035485

16

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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).

17

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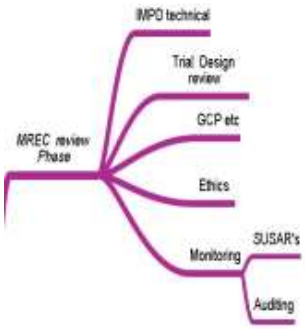
MREC Review Phase



Needed:

- Knowledge
  - GMP, GCP, GLP etc.
  - Product development
  - IMPD
  - Etc
  - = TEAMWORK
- Critical Attitude
- Time

18

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

19

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Trial Implementation Phase

Needed:

- GMP/GCP facilities
- GCP approved quality system
- GMP/GCP trained personnel
- Knowledge
  - GMP, GCP, GLP etc.

  = TEAMWORK

20

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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

Professional Guidance on Pharmacy Services for Clinical Trials 1, October 2013 National Pharmacy Clinical Trials Advisory Group, Royal Pharmaceutical Society

21

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What you get in return:

- Cooperation with physicians etc..
- Knowlegde
- Cooperation with MREC members
- Frontline of new developments

22

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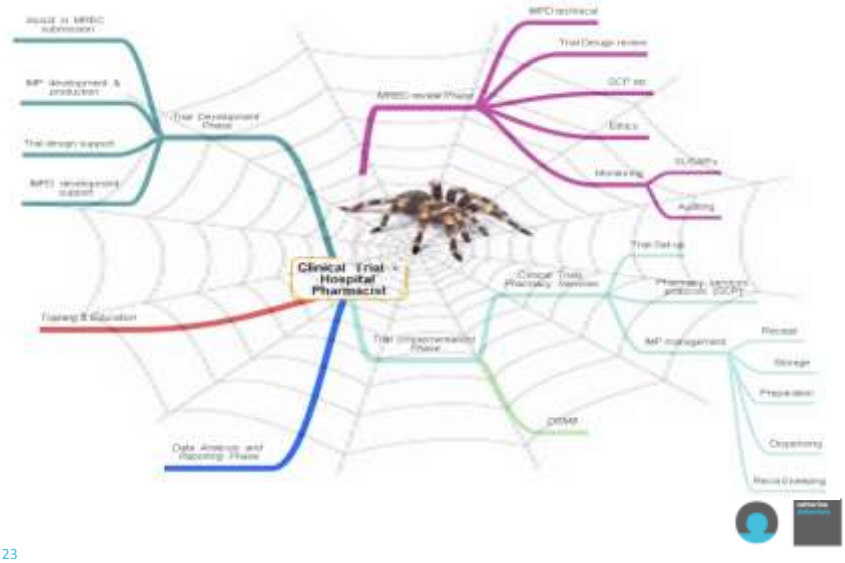

23

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Thank You

24