REGULATORY REQUIREMENTS FOR CLINICAL TRIAL APPROVAL – MEDICAL DEVICES

DR D DIALE
MRS P NKAMBULE

02 December 2015
Background to clinical trials

Stakeholders in clinical trials

Legislative requirements

Guidelines

Key aspects for clinical trial approval

Conclusion
South Africa provides unique, highly attractive research environment

- Diverse population
- Well developed skills, expertise and infrastructure
- Number of clinical trials increasing
- Increasing research activity and competition for research
- Communities are largely marginalised with limited understanding of scientific research and ability to provide informed consent (11 official languages)
- Ethical monitoring systems
- Over-researched communities
- Most trials in private sector - ?? Capacity building
Stakeholders in clinical trials

- MEDICINES CONTROL COUNCIL (MCC)
- SPONSOR / CRO
- LOCAL ETHICS COMMITTEE
- TRIAL PARTICIPANT
- INVESTIGATOR

This diagram illustrates the various stakeholders involved in clinical trials, including the Medicines Control Council (MCC), sponsor or CRO, local ethics committee, trial participant, and investigator.
## Stakeholder Expectations

<table>
<thead>
<tr>
<th>MCC/MRA</th>
<th>PARTICIPANT</th>
<th>APPLICANT/PI</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Efficient System where applications submitted comply:</td>
<td>• Access to devices that are:</td>
<td>• Speedy, efficient processing of application</td>
</tr>
<tr>
<td>➢ Quality Submissions</td>
<td>✓ safe,</td>
<td>• Better communication</td>
</tr>
<tr>
<td>➢ Ethical</td>
<td>✓ perform and</td>
<td>• Remain competitive and</td>
</tr>
<tr>
<td>➢ Patients Safety assured</td>
<td>✓ of good quality</td>
<td>• Financial Viable</td>
</tr>
<tr>
<td>➢ GCP compliance</td>
<td>• Clinical trials conducted that:</td>
<td></td>
</tr>
<tr>
<td>➢ Accountability</td>
<td>➢ ensure participant safety</td>
<td></td>
</tr>
<tr>
<td></td>
<td>➢ respect for participant rights and</td>
<td></td>
</tr>
<tr>
<td></td>
<td>➢ are ethical</td>
<td></td>
</tr>
</tbody>
</table>
Legal framework

- Medicines Control Council (MCC): established in terms of Sec 2 of the Medicines and Related Substances Act 1965 (Act 101 of 1965)

- National Health Research Ethics Council: Established in terms of the National Health Act 2003 (Act 61 of 2003) (Sec. 9) It registers all Ethics Committees; Also has guidelines (2004)

- Local Ethics Committees: Also established in terms of the Health Act (Sec 9) review research proposals and protocols and grant approval for those that meet ethical standards

- SA GCP and other international guidelines
Legal framework

- Medicines Control Council (MCC)
- National Health Research Ethics Council (NHREC)
- Local Ethics Committee
- Regulation of Clinical Trials
- SA GCP and other international guidelines
Medicine Act (Act No, 101 of 1965), Bill 6

Section 2B (f) – Functions of the Authority
Section 21 - Authorize sale of unregistered medical device or IVD for certain purposes
   Exemption for import and use of unregistered medical device or IVD

Section 21 authorisation letter: MCC approval letter: import licence for quantity of investigational product requested in application form.

National Health Act (Act No, 61 of 2003)
Section 90 allows for the establishment of Regulations that prescribed GCP guidelines.
REGULATION 17: CONDUCT OF CLINICAL TRIALS AND CLINICAL INVESTIGATIONS

17(1) A person desiring to initiate or conduct a clinical trial or clinical investigation in respect of an unregistered medical device or performance assessment for an IVD, or a new intended purpose of a registered medical device or IVD, shall apply to the Council on a form determined by the Council for authorization to conduct such a clinical trial or clinical investigation.

17(4) Clinical investigations and clinical trials must be conducted in accordance with guidelines for good clinical practice determined by the Council.

17(5) No person shall conduct clinical investigations or clinical trials referred to in subregulation (1) without the authorisation of the Council.
17(6) – The person conducting the clinical investigation or clinical trial must:

➢ submit progress reports to the Council after every six months from the date when the clinical investigation or clinical trial was started and 30 days after the completion or termination of the clinical investigation or clinical trial;

➢ submit adverse event reports immediately or as soon as practically possible to the Council.

17(7) – The Council may request additional information, inspect a clinical investigation or clinical trial or withdraw the authorisation to conduct a clinical investigation or clinical trial if the Council is of the opinion that the safety of the subjects of the clinical investigation or clinical trial is compromised, or that the scientific reasons for conducting the clinical investigation or clinical trial have changed.
17(8) – The following information for a medical device or IVD referred to in sub regulation (1) shall be provided, where applicable;

a) Intended purpose or use of the investigational device in the proposed clinical investigation or clinical trial.

b) The populations and indications for which the investigational device is intended.

c) Name or number of the model or type, including software version and accessories, if any, to permit full identification.

d) Description as to how traceability shall be achieved during and after the clinical investigation, (e.g. by assignment of lot numbers, batch numbers or serial numbers).

e) The medical device or IVD shall, where practical, be labelled with the name(s) and address(es) of the premises where the clinical investigation or clinical trial is to be carried out and be labelled “for investigational use”.


- support the regulatory requirements of the MCC and regulations related to Health Research in the National Health Act.

- applicable to both academic and contract clinical research.


3. International Guidelines
GCP Principles

1.2.1. Study Rationale and Motivation
1.2.2. Study Designs
1.2.3. Investigator Competence
1.2.4. Balance of Harm and Benefit
1.2.5. Transparency
1.2.6. Privacy
1.2.7. Ethical Review
1.2.8. Informed Consent
1.2.9. Safety Monitoring
1.2.10. Multi-centre Studies
Established by Minister of Health in 1999

Provides legal framework for the review of clinical trials

Reviews and recommends approval of the conduct of clinical trials

Bioequivalence studies

GCP inspectors of trial sites

Approves Sec 21 Applications (unregistered medical devices) for compassionate use
An application to Ethics Committee & registration with South African National Clinical Trials Register (SANCTR) in parallel to MCC submission

2 bound copies of submission (documents as outlined in second page of CTF1, including 2 electronic copies)

Confirmation of payment for processing of application(s)

- clinical trials (Companies): R9000;
- clinical trials (Institutions): R4500;
- any other clinical trial: R2200;
The purpose of the CTF1 is to assist members of the Clinical Trials Committee to determine the answers to the following questions:

- Does this proposed trial contribute to new knowledge in a scientific way?
- Are all aspects of the proposed trial ethical?
- Can patient safety be assured?
- Should this trial be done in SA?

The application is divided into three sections.

- **Section 1:** A checklist of required documentation. (If the documentation is incomplete, the application will not be further processed.)

- **Section 2:** Administrative and Supplementary Details.

- **Section 3:** Applicant’s Report / Presentation
Key Aspects for Clinical Trial Approvals

In the approval of Clinical Trials the MCC considers the following aspects:

a. Scientific rationale

b. Safety

c. Contribution to new scientific knowledge

➢ Is it ethical, relevant and can patient safety be assured?
➢ When the trial is undertaken in South Africa, the subjects should benefit from the results of the research
Key Aspects for Clinical Trials cont.

**SCIENTIFIC RATIONALE**

- Does the trial contribute to new scientific knowledge?
- Is it scientifically appropriate?
- Is the study design optimal?
- Should the trial be conducted in the RSA?
- Is there adequate pre-clinical evidence of safety and performance?
SAFETY

- Balance of risks versus benefits
- Is there adequate data from preclinical studies?
- Are the animal models used appropriate?
- Is there adequate monitoring in place? Are the investigators over-committed?
- Vigilance and GCP inspection reports
- Is safety stipulated as an objective?
RECOMMENDATIONS TO MCC

B8.1 technical document is tabled at MCC with a summary reports and recommendations stratified by decision category:

1A: Approved – nothing outstanding
1B/2A: Ethics and admin. queries - responses approved “in house”
2B: Technical queries, responses to be sent to reviewer
3: Responses to be deliberated by full CTC committee
4: Referral to expert outside committee
5: Non approval (Quality, design, unethical) - resubmit
6: Rejected at screening (missing docs) - resubmit

B8.2 Section 21 applications (line listing)
B8.3 Clinical trial GCP inspections
MCC Approval

Research Ethics Committee Approval

Submissions to MCC and Ethics committee could be done in parallel

Recording on South African National Clinical Trials Register (SANCTR)