Regulatory Requirements for Clinical Trials & Legal Framework

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National Medicines Regulatory Authority

In summary .....

- Objectives
- Sub Committee on Clinical Trials (SCOCT)
- Type of trials currently regulated
- Procedure
- Documents required
- Legal Framework

Objectives of regulating clinical trials

- **Protecting rights, safety and wellbeing of trial subjects**
  - Involvement of human as subject trial
  - Involves many stakeholders
  - Includes trials to prove the efficacy and safety of new medicine, including biological medicine
  - The use of trial product, not yet registered
  - Quality of product

Objectives of regulating clinical trials

- **Trials that collect high quality, credible data**
  - NMRA does not approve first-time medicines
  - NCEs – require MA by a reference DRA for two years
  - Multicenter trials generate data required for reference DRAs
  - Reference authorities would not accept data from unregulated countries

SCOCT

- **Sub Committee on Clinical Trials**
  - Established in January 2009 under CDDA
  - Continues to function under NMRA
  - 13 members consist of Academics, Clinicians, Medical Administrators & Pharmacists
  - Meet monthly

Role of SCOCT

- **Provides regulatory oversight**
  - Reviews and recommends trial applications
  - Ensures implementation of Good Clinical Practice (GCP) standards
  - Monitors safety & wellbeing of clinical trial subjects.
  - Develops and implements guidelines and SOPs for relevant regulatory activities.

What does SCOCT regulate?

Definition for a clinical trial

- A prospective study comparing the effects of an intervention against a control in human subjects.

Interventions

- Health related interventions
  - Pharmaceutical products
    (Medicines, Vaccines, Biological Products)
  - Medical devices
  - Surgical procedures
  - Radiological procedures
  - Any other items claimed to have therapeutic benefits

What type of clinical trials

Clinical trials involving

- Unregistered medicines (NCEs)
- Registered medicines – outside conditions of registration
  - Indication
  - Target patient population
  - Route of administration
  - Dosage regimen

Trial Phases

- Phase I trials are not allowed
- Phase II, III and IV trials can be allowed
- Phase II

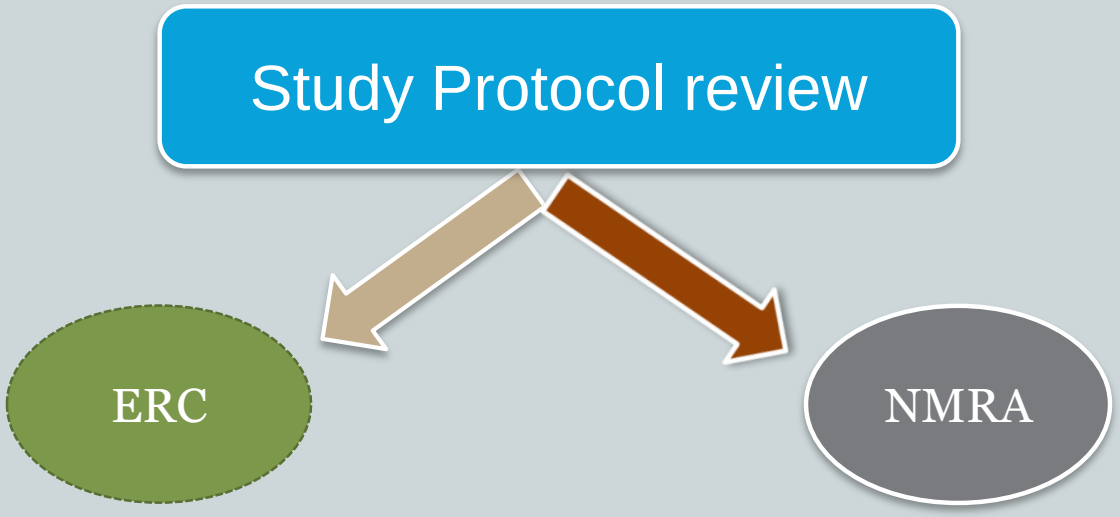
  If same study protocol is approved by a benchmark regulatory authority,

  WHO sponsored trials

Benchmark Authorities

- USFDA, USA
- Health Canada, Canada
- MHRA, United Kingdom
- EMA, European Union
- TGA, Australia
- Medsafe, New Zealand
- PMDA, Japan
- HSA, Singapore

Procedure



- (Ethics review) (Regulatory review)

Regulatory Review

- Application to NMRA in triplicate
- Suitably qualified Principal Investigator(s)
- At present, no fee involved
- Initial screening by NMRA
- SCOCT decides on expert reviewers
- Final decision based on reviewers' recommendations
- NMRA issues letter of approval

Regulatory Requirements

- Documents
- Qualified investigators
  - Registered Medical or Dental Practitioners
  - Experienced in carrying clinical trials
  - GCP trained and certified
  - Should be familiar with the appropriate use of IMP as described in trial documents
  - Should have access to such investigational and treatment facilities
- Ethical approval
- Registration in SLCTR

Required Documents

- Clinical Trial Protocol
- Investigators Brochure (IB)
- Curriculum vitae of Investigators
- Information Sheets & Consent Forms (In three languages)
- Certificate of liability insurance
- Approval from a recognized Ethics Committee
- Approval letter from head of the institute where trial is done
- GMP certificate and certificate of analysis for the IMP
- Regulatory status in other countries

Ethics Review Committees

SLMA

FoM Colombo

FoM Jaffna

FoM Kelaniya

MRI

FoM Peradeniya

FMS Jayewardhanapura

FoM Ruhuna

Colombo, Jayewardhanapura, Peradeniya, & SLMA - accredited by **SIDCER**

(Strategic Initiative for developing capacity in Ethical Committees)

Clinical Trial Protocol

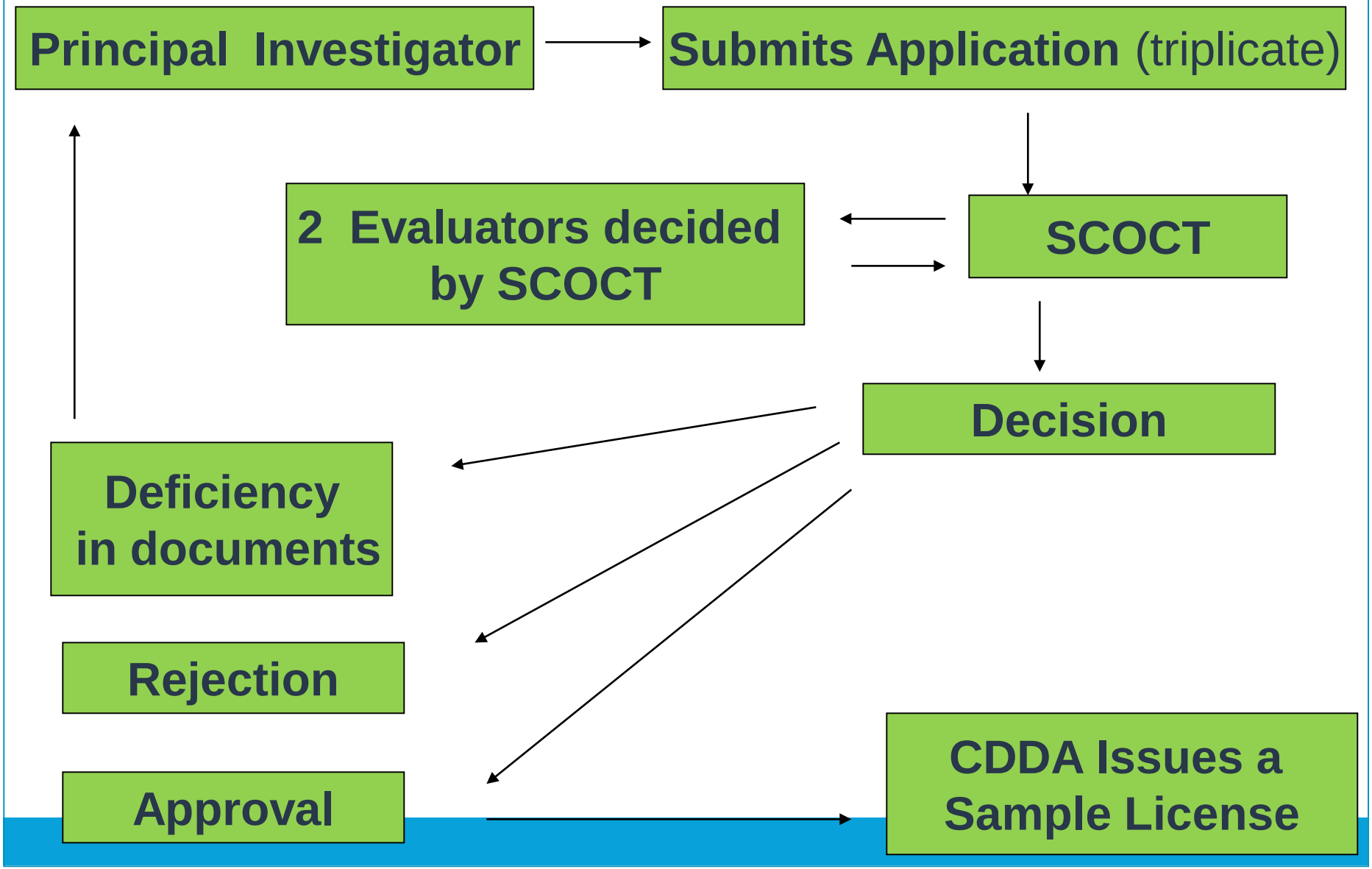
- Background, rationale & objectives of the trial
- Trial design, methodology & organization
  - Well defined outcome measure
  - Well defined population and period of observation
  - Details of sites, sponsor, Independent data monitoring committee (IDMC), data safety monitoring board (DSMB)
- Protocol should be dated and signed by the PI

Investigator's Brochure (IB)

Data related to investigational product(s)

- Chemical and pharmaceutical data
- Animal pharmacology & toxicology data
- Specific pharmacological actions
- Pharmacokinetic data
- Available human clinical pharmacology data

Procedure


Principal Investigator
Submits Application (triplicate)
SCOCT
2 Evaluators decided by SCOCT
Decision
Deficiency in documents
Rejection
Approval
CDDA Issues a Sample License

After approved ....

- Approval/NOL should be obtained from the head of the institution of the trial site
- Trial should be registered in Sri Lanka Clinical Trials Registry (a primary clinical trials registry of the WHO)
- Sample licenses will be issued to import investigational products and ancillary items on payment of a prescribed fee

Ongoing submissions

- Protocol changes
- Amendments to other trial related documents (e.g. IB, ICF)
- Deviations to the protocol
- Reports of Serious Adverse Events
- Decisions of the DSMB, emerging safety data which would effect participating subjects adversely
- Progress reports every six months

Changes that require regulatory approval

- Change of Principal Investigator if he is the holder of the approval
- Substantial amendments to the protocol which are likely to have a significant impact on
  - Safety of the patients
  - Scientific value of the trial
  - Conduct or management of the trial
  - Quality & safety of the IMP

Status Reports

- Ongoing (every six months)
- Premature site closure
- Suspension
- Termination
- Completion
  - Final report with summary of trial's out come
  - Reasons for premature site closure/ termination
  - Details relevant to destroying of balance study material

Legal Framework

- Cosmetics Devices and Drugs Act (CDDA) No 27 of 1980 and its regulations
- National Medicines Regulatory Authority Act No 05 of 2015

CDD Regulations

IMPORT OF DRUGS FOR TEST, EXAMINATION, DISTRIBUTION AS SAMPLES, ANALYSIS AND CLINICAL TRIAL

24. (1) Every person desirous of obtaining a license to import small quantities of any drug for test, examination, distribution as samples or clinical trial, shall make a separate application to the Authority in respect of each drug he intends to import. Every such application shall be substantially in Form C of schedule V hereto.

(2) No person shall import samples of any drug specified in schedule 111 hereto.

(3) Every applicant for a license to import any registered drug shall furnish to the Authority all such information as the Authority may require for the purpose of enabling the Authority to dispose of such application.

NMRA Act

Objectives of the Act

(d) encourage the manufacturing of good quality medicines in Sri Lanka with a view to assuring the availability of essential medicines at affordable prices;

(*e) promote the safe and rational use of medicines,* medical devices and borderline products by health care professionals and consumers;

(*f) recommend appropriate amendments to relevant* laws pertaining to medicines, medical devices and borderline products;

(*g) educate the general public, health care* professionals and all stakeholders on medicines, medical devices and borderline products;

(*h) regulate the promotion and marketing of* medicines, medical devices and borderline products;

(*i) regulate the availability of the medicines,* medical devices and borderline products;

(*j) conduct post marketing surveillance on quality,* safety and adverse reaction of the medicines,

medical devices and borderline products; and

(*k) regulate all matters pertaining to the conduct of* clinical trials in Sri Lanka.

Divisions of the Authority

National Medicines Regulatory Authority
Act, No. 5 of 2015

(iii) Medical Devices Regulatory Division which shall be responsible for regulation and control of all aspects pertaining to medical devices as may be authorized and directed by the Authority;

(iv) Borderline Products Regulatory Division which shall be responsible for regulation and control of all aspects pertaining to borderline products as may be authorized and directed by the Authority;

(v) **Clinical Trials Regulatory Division** which shall be responsible for regulation and control of all aspects pertaining to clinical trials carried out in Sri Lanka as may be authorized and directed by the Authority;

(vi) Information, Education, Communication and Research Division which shall be responsible for educating the people as well as stake holders and healthcare professionals on rational use of medicines, medical devices and borderline products and promoting research into medicines, medical devices and borderline products as may be authorized and directed by the Authority;

(vii) Inspectorate and Enforcement Division which shall be responsible for inspecting and investigating issues pertaining to proper implementation of the provisions of this Act as may be authorized and directed by the Authority;

(viii) Pharmacovigilance Division which shall be responsible for monitoring and dealing with adverse drug reaction, quality failure and counterfeit medicines as may be authorized and directed by the Authority;

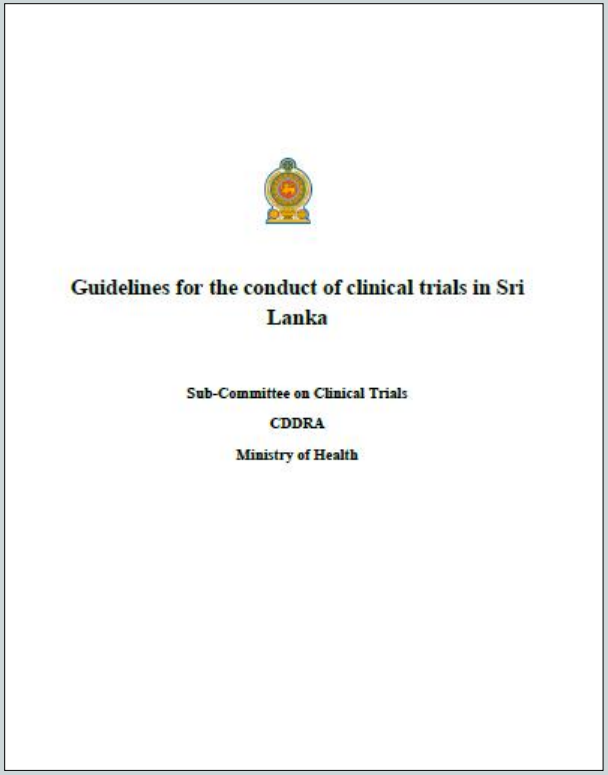
(ix) Pharmacies Regulatory Division which shall be responsible for the regulation and control of pharmacies in Sri Lanka as may be authorized and directed by the Authority;

The future

- Strengthening of regulations and guidelines
- Establishment of the Clinical Trials Regulatory Division
- Directing Ethics committees to get WHO accreditation
- Development of human resources capabilities

Our web site
cdda.gov.lk

- Clinical Trials Guidelines



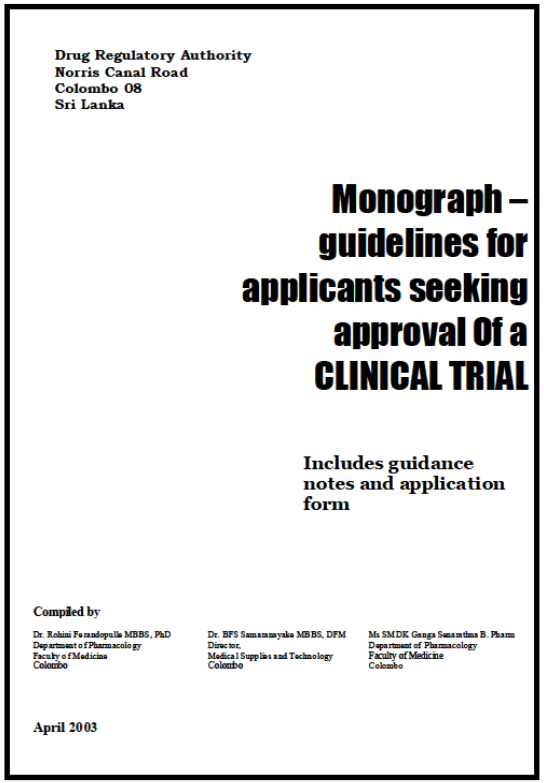
Guidelines for the conduct of clinical trials in Sri Lanka

Sub-Committee on Clinical Trials

CDDRA

Ministry of Health

- Application



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Colombo 08
Sri Lanka

Monograph – guidelines for applicants seeking approval Of a CLINICAL TRIAL

Includes guidance notes and application form

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Thank you