Sponsor:

An individual, company, institution or organization which takes responsibility for the initiation, management and/or financing of a clinical trial.

Responsibilities:

1. Quality Assurance and Quality Control
2. Contract Research Organization (CRO)
3. Medical Expertise
4. Trial design
5. Trial management, data handling and record keeping
6. Investigator selection
7. Allocation of Responsibilities
8. Compensation to subjects and investigators
9. Financing
10. Notification/Submission to Regulatory Authority
11. Confirmation of review by IRB/IEC
12. Information on investigational products
13. Manufacturing, packaging, labeling and coding investigational product(s)

14. Supplying and Handling investigational Product(s)
15. Record Access

1- Quality Assurance and Quality control:

- The sponsor is responsible for implementing and maintaining quality assurance and quality control systems with written SOPs to ensure that trials are conducted and data are generated, documented (recorded), and reported in compliance with the protocol, GCP, and the applicable regulatory requirement(s).

2. Contract Research Organization (CRO):

- A sponsor may transfer any or all of the sponsor's trial-related duties and functions to a CRO, but the ultimate responsibility for the quality and integrity of the trial data always resides with the sponsor. The CRO should implement quality assurance and quality control.

3. Medical Expertise: برگزیدن، معتمدن

• The Sponsor should designate appropriately qualified medical personnel who will be readily available to advise on trial related medical questions or problems.

4. Trial design:

• The Sponsor should utilize qualified individuals (e.g. biostatisticians, clinical pharmacologists, and physicians) as appropriate, throughout all stages of the trial process, from designing the protocol and CRFs..and planning the analyses to analyzing and preparing interim and final clinical trial reports.

5. Trial management, Data Handling, and Record keeping:

• The Sponsor should utilize appropriately qualified individuals to supervise the overall conduct of the trial to handle the data to verify the data to

...

conduct the statistical analyses, and to prepare the trial reports.

6. Investigator selection:

- The sponsor is responsible for selecting the investigator(s); Each investigator should be qualified by training and experience and should have adequate resources to properly conduct the trial for which the investigator is selected.

7. Allocation of responsibilities:

Prior to initiating a trial, the sponsor should define, establish and allocate all trial-related duties and functions.

8. Compensation to subjects and investigators:

- If required by the applicable regulatory requirement(s), the sponsor should provide insurance or should identify (legal and financial coverage) the investigator the institution against

claims arising from the trial, except for claims that arise from malpractice and/or negligence.

9. Financing:

- The financial aspects of the trial should be documented in an agreement b/w the sponsor and the investigator.

10. Notification / Submission to regulatory Authority:

- Before initiating the clinical trial(s), the sponsor (or the sponsor and the investigator) if required by the applicable regulatory requirement(s) should submit any required application(s) to the appropriate authority(ies) for review, acceptance and/or permission (as required by the applicable regulatory requirement(s)) to begin the trial(s).

11. Information on investigational Product(s)

- When planning trials, the sponsor should ensure that sufficient safety and efficacy data from

...

nonclinical studies and/or clinical trials are available to support human exposure by the route at the dosage for the duration and in the trial population to be studied.

12. Manufacturing, Packaging, labeling and coding investigational Product(s):

- The sponsor should ensure that the investigational product(s) (including active comparator(s) and placebo, if applicable) is characterized as appropriate to the stage of development of the product(s) is manufactured in accordance with any applicable GMP and is coded and labeled in a manner that protects the blinding, if applicable.
- In addition, the labeling should comply with applicable regulatory requirement(s).

13. Supplying and Handling investigational Product(s)

- The sponsor is responsible for supplying the investigator(s) with the investigational product(s).

□ Investigator:

A person responsible for the conduct of the clinical trial at a trial site. If a trial is conducted by a team of individuals at a trial site, the investigator is the responsible leader of the team and may be called the principal investigator.

◦ Sponsor-investigator:

An individual who both initiates and conducts alone or with others a clinical trial, and under whose immediate direction the investigational product is administered to, dispensed to, or used by a subject.

◦ Sub investigator:

Any individual member of the clinical trial team designated and supervised by the investigator at a trial site to perform critical trial-related procedures and/or to make important trial-related decisions (e.g. associates, residents, research fellows).

□ Investigators' Responsibilities:

1. investigators Qualifications

2. Adequacy of Resources
3. Medical care of Study Participants
4. Communication with the IRB/IEC
5. Compliance with the Protocol
6. Investigational Product Care
7. Randomization and unblinding proceed (2M)
8. The informed consent
9. Records and Reports
10. Progress reports
11. Safety reporting
12. Stopping or suspending a study
13. Final report

1. Investigators Qualifications:

- Properly qualified to assume the responsibilities for conduct of the study.
- Very familiar with the drug under investigation
- Will comply with regulations and be prepared for audits and monitoring
- Has available detailed list of all to whom responsibility is delegated.

2. Adequacy of resources:

- Can recruit SP in sufficient numbers and on time
- There is enough time to complete the study
- There are enough qualified staff and adequate facilities to complete the study.
- The staff are well informed about the Test Agent and the Protocol.

3. Medical Care of Study SP Participants:

- All medical decisions are made by qualified physicians
- All medical acts are performed by qualified physicians
- The investigator is responsible for care of SP when there are "Adverse Events"
- The primary physician of the SP is notified regarding the participation of their patient on the study.
- The Study Physician knows when and why a Study Participant leaves a study accounting for all SP.

4. Communication with the IRB/IEC:

- Written approval is obtained before the study begins

- informed consent is in the language of the SP
- The IRB has a current investigators Brochure
- The IRB has all documents when needed
- Protocol amendments are submitted on time
- The IRB/IEC gets an annual report of each study

5. Compliance with the Protocol:

- Has Signed Protocol confirming agreement to comply with it to the letter
- Has not deviated from the Protocol without written agreement from the Sponsor and the IRB/IEC.
- Has documented each and every deviation (for Subject Safety reasons) from the protocol when it occurs.
- Implements deviations to avoid risk but immediately submits amendments to IRB, Sponsor and the FDA.

6. Investigational Product Care:

- Accepts responsibility for the products, its usage and its

Storage according to the Protocol.

- Only a Pharmacist involved under PI's supervision
- Explains to SP, and uses test agent, properly only
- Detailed records of test agents are kept throughout the study
- Retained unused test agent and destroy only under the written instruction from the Sponsor

7. Randomization and unblinding procedure:

- The study randomization procedures (documented in the protocol) are followed exactly.
- The randomization code is only broken in accordance with the protocol
- If the study was blinded, any unblinding was documented and Sponsor notified in writing.

8. The informed consent

- Insure that the declaration of Helsinki and the principles of GCP are adhered to
- Insure that there is no coercion of subjects to

be on, or stay on, a study at any time

- Insure SP understanding of the information they are presented by you or your designees
- Insure that the informed consent is signed and dated by the SP or SP's legal representative.

9. Records and Reports:

- Data is ALCOA (accurate, legible (خوانا، روشن), contemporaneous (هم‌زمان), original and attributable (نسبت دادن)) and complete
- Data on the CRF's is consistent with (exactly the same as) that of the source documents (raw data)
- All changes to a CRF are dated and signed such that the original data is not obscured (مبهم کردن)
- Essential documents are retained (نگاه داشتن) at least 2 years after the last approval of the test agent for market.

10- Progress Reports:

- A written report is submitted to the IRB/IEC at least annually is required but
  - Low Risk - yearly is ok
  - Moderate Risk - twice a year
  - High Risk - monthly to quarterly as needed...

- A written report is submitted to the IRB/IEC if the PI notes any change that might significantly change the conduct of the trial.

11. Safety Reporting

- All SAE's are immediately reported to the Sponsor and followed up by a written report forthwith (immediately)
- Study Participants are not to be identified to anyone
- All AE's critical to the safety evaluation are reported to the Sponsor per protocol.
- The Sponsor and the IRB are given all details in the event of a death of a SP while on study.

12. Premature Stopping or Suspending a Study:

- All SP are informed if a Study is terminated or even Suspended.
- The institution, the Sponsor and the IRB are informed in writting if the PI terminates the study.
- The institution and the IRB are informed in

writting if the sponsor terminates the study
- The institution and the sponsor are informed in writting if the IRB terminates the study.

13. Final Report(s) by investigator:

- The Principal investigator is expected to file a written report at the conclusion (انتهاء، انتهى) of a study.

Final Report:

- Upon completion of the study the investigator must notify the IRB and the sponsor.
- The final report should contain the introduction, description of the methods, results and discussion of the finding.

□ Definitions:

◦ Sponsor:

An individual, company, institution, or organisation which takes responsibility for the initiation, management and/or financing of a clinical trial.

◦ Contract Research Organisation:

An individual or organisation which are contracted by the sponsor to conduct one or several of the sponsor's trial related duties and functions. The ultimate responsibility for the quality and integrity of the trial data always resides with the sponsor (GCP).

□ Contract Research Services:

◦ Product development

◦ Clinical research management (pre-clinical-phase IV)

- Clinical, medical, security monitoring
- Toxicology
- laboratory services
- Data management
- Bio Statistics
- Consulting services associated with Government agencies
- licensing procedures
- Medicine management (production, packaging, labeling, storage, distribution, collection)
- Researchers and central services choice

etc.

CRO choice:

- Clinical research, must be done basing on the written rules of: ICH-GCP, Declaration of Helsinki, GMP, GDP, local regulations and guidelines.

According to ICH-GCP related to the CRO;

5.2.1 The sponsor may transfer all or a portion of duties and functions associated with its own to the Contract Research Organizations. However, the ultimate responsibility of the quality and accuracy of research data always belongs to the sponsor. Contract Research Organization has to apply quality control and quality assurance system.

5.2.2 Any task or function transferred or taken over from the Contract Research Organizations has to be specified in writing.

5.2.3 The responsibility of any task or function specially not transferred or taken over from the Contract Research Organizations belongs to the sponsor.

. 5.2.4 Refers made to the sponsor in the user guide, to the extent of task or function transferred or taken over from the Contract Research Organizations also does include the Contract Research.

. The sponsor has to be sure of the quality of service received and having required experience and knowledge of the duties, that are transferred from SAK. For this reason, many sponsors have created criteria to work with CRO who have these competencies.

. Some of these criteria are;

→ experience from similar projects of the CRO
→ experience with similar sponsors of the CRO
→ For how much years the CRO is working in this area.

→ training and experience of staff with clinical research

→ Compliance and information with local regulations

→ Software used

- Making a contract with the CRO:

The sponsor after primarily determining needs of its own research has to make a contract with the CRO for the transfer of tasks related to these services.

This contract has also to contain:

legal issues such as contract work directive, the service time, time of payment, amount etc (obligations, insurance, termination, choice of law etc).

• CRO responsibilities:

. CRO training programs should be created for new joining organizations.

. If services should be taken from outside, assessment process should be available.

. CRO training programs should be created for service taken from people/organizations from outside.

. It should have appropriate personnel, infrastructure and facilities to meet the requirements of the project.

. It should have the necessary software to monitors and measure Project management and performance.

. It should be made sure that the insurance made by the sponsor is appropriate.

. The application file provided by the sponsor

should be careful reviewed and compliance must be ensured.

- It should be made sure that Medicines process is managed well (place and conditions of the place where drugs are being manufactured, in which conditions they are stored, how the distribution is made, shelf life, tags, etc).
- For Protocol or research brochure revision, process must be defined.
- If there is transfer of the task, it must be well documented.
- Routine quality control of the System must be created.

Contract: قرارداد، قراردادبستن

Contract Research Organisation (CRO)

A person or an organisation contracted by sponsor to perform sponsor's trial related duties and functions.

- FDA definition: CRO is a person, an independent contractor (پیمانکار) of sponsor

- One or more obligations (وظیفه) of sponsor such as:
  - → design of Protocol
  - → Selection of research site
  - → Monitoring of investigators
  - → Evaluation of study data
  - → Preparation of materials to be filled ē FDA.

Services: Protocol development
- Site/investigator recruitment and selection
- Personal training
- Clinical trial management
- Quality assurance and site monitoring
- Data analysis
- medical writing
- Processing and preparing regulatory filling and liaison ē regulatory bodies

Contract Research Organization

#Responsibilites of CRO:

- CRO work in a team under direct supervision of principal investigators.

A- General Responsibilities:

a- Capacity building
b- training new CROs

a- Capacity building:

Work of CRO begins the day he joins employment whether or not sponsor has selected an investigator site for any particular trial.
They conduct an indep survey of new sites. to assess:

- Manpower presence or competence
- Support staff
- Infra structure
- Presence of functional ethics committee
- Compatible management
- Major disease - incidence + prevalence rate

b- Training new CROs:

Experienced CRO → train new CROs

training conducting
- Feasibility studies
- designing trial document
- Setting up of Sites
- Conduct of trial
- trial close out

B- Trial-related Responsibilities: P_2PST

a- Site identification

b- Pre trial documentation

c- Financial Responsibilities

D- Training the site Staff

E- Post trial activities

[redacted]

. To identify right site for trial → Fulfil all criteria by protocol.

- CRC understand { needs, Expectations, Potential of the site

Pretrial documentation

CRC collect updated and signed resume of each member of site ...

Pretrial documents
1. Form 1572
2. Financial disclosure form
3. undertaking from principal investigator
4. Confidentiality non-disclosure agreement
5. Coordinating ē IRB

CRC must ensure that pretrial documents are completed within specified timeline.

Financial responsibilities

گفت وگو کردن، به قبول نفد تبدیل کردن
Senior CRC negoticate the trial budgets at the site. includes: ◦investigators fees
- ◦IRB fees
- ◦Site adminstration fees
- ◦lab cost
- -Study subject travel

(D) [redacted]

CRC train the site staff

Can highlight on
- → inclusion criteria
- → Exculsion criteria
- → schedule of visits
- → window period
- → Visit specific activities
- → Safety guidlines and reporting timeline as per protocol.

(E) [redacted]

Once hospital phase of trial is over. completely study documentation will become important

They do
- final check CRFs (case report forms)
- maintain an archival inventory of records

□ Potential advantages of CROs:

- Reduce time needed to develop a new drug
- Reduce sponsor's fixed cost associated with personnel, equipment and facilities
- Provide knowledge of regulatory climate in foreign markets.

Clinical Research Associate (CRA):

-Also called a clinical monitor or trial monitor, is a health-care professional who performs many activities related to medical research, particularly clinical trials.

- Clinical research associates collect and organize data obtained during studies and trials conducted in fields, such as biotechnology and pharmaceuticals.

- CRA
  - ensures compliance ē protocol
  - check clinical site activities
  - make on-site visits
  - reviews CRFs
  - Communicates ē investigators

As per ICH-GCP guidline:

-Monitors should be appointed by sponsor.
-Monitors should be trained, have scientific and clinical knowledge.

- A monitor's qualifications should be documented.
- Monitors should be familiar ē { Investigational products
  Protocol
  written informed consent form

□ Monitor's Responsibilities:

1- Acting as main line communication b/w sponsor and investigator.

2. Verifying that investigator has adequate qualification and resources facilities including { laboratories
  equipment
  staff
  adequate safety ---

3- Investigational product: that storage time and condition are acceptable.

4. that investigational products are supplied only to subjects who are eligible to recieve it and at protocol specified dose.

5- Subjects are provided ē necessary instruction on using, handling, storing.

6. Disposition of unused investigated products at trial sites. complies c applicable regulatory and is in accordance c sponsor.
7. Verifying that investigator follows approved protocol and all approved amendment.
8. Verifying that written informed consent was obtained before each subject's participation in trial.
9. Ensuring that investigator recieves (current investigator brochure.
10- Ensuring that investigators trial staff are performing.
11- Verifying the investigator is enrolling only eligible subjects
12. Reporting the subject recruitment rate.
13. Verify documents and trial records are accurate, complete and up to date.
14. Verify that investigators provides all required reports, notification, application and these documents are accurate, complete

15. Checking the accuracy and completeness of CRF entries, source documents and related records.

16. Any dose and therapy modifications are well documented for each trial subject.

17. Adverse event, contamitant medication and intercurrent illnesses are reported ē protocol on CRFs.

Auditors:

Audit:

A Systematic and independent examination of trial related activities and documents to determine whether the evaluated trial related activities were conducted, and the data were recorded, analyzed and accurately reported according to the protocol, sponsor's standard operating procedures (SOPs), Good Clinical Practice (GCP), and the applicable regulatory requirements

Audit Certificate

A declaration of confirmation by the auditor that an audit has taken place.

Audit Report

A written evaluation by the sponsor's auditor of the results of the audit.

Audit Trail

Documentation that allows reconstruction of the course of events.

Auditors

• Selection and Qualification of Auditors

a- The sponsor should appoint individuals, who are independent of the clinical trials/systems to conduct audits.

b- The sponsor should ensure that the auditors are qualified by training and experience to conduct audits properly. An auditor's qualifications should be documented.

□ Responsibilities of Auditors:

The Sponsor should specify the roles and responsibilities of the auditor before starting to conduct an audit so as to ensure fair and smooth performance of the audit. The auditor is responsible for maintaining the confidentiality of information obtained during an audit, planning (designing and updating) and conducting the audit, and reporting the audit results.

□ Purpose of Audit:

To evaluate the trial conduct and compliance with:

i. Quality Systems

ii. SOPs

iii. Protocol

iv. Good clinical practice and

v. Other applicable regulatory requirements

□ What to audit?

- Organization and personnel responsibilities and functions.
- Qualification, training and adequacy of staff list of monitors, List of all investigators
- Drug supply agreement, clinical trial(site) agreement, other services agreement and material transfer agreement.

- Quality management system
- Investigational drug
  - Manufacturing
  - Packaging
  - labeling and coding of the IP (including placebo and active comparator where applicable) in accordance with applicable GMP standards Labeling requirements.
- Drug product Accountability
- IRB/IEC
  - responsibility
  - composition
  - functions
  - operations
  - Procedures
  - Records

- Essential documents:
  - → Investigator's brochure
  - → Signed protocol and amendments (How are changes and deviations to the protocol handled?)
  - → Advertisements for subject recruitment
  - → Informed consent forms, Approved by IRB/IEC? (All been signed off according to requirements
  - → Financial aspects of the trial
  - → Case report forms
  - → Serious adverse events reporting
  - → instructions for handling
  - → Shipping records
- Bio-analytical laboratories
- Computerized Systems
- Statistical components

• How to execute an audit?

→ The execution of audit process is divided into three steps:

i- Before the audit

ii- During the audit

iii- After the audit

□ Before the audit process:

- Auditor contacts the site to arrange for a mutually acceptable date and time for an audit to be conducted.
- A detailed agenda of an audit is informed to the CRC and also about the documents to be checked during an audit.
- Auditor previews the protocol, CRF, local regulations and guidelines, project

specific guidelines, relevant SOPs to be aware of the trial.

□ During the audit process:

- Opening meeting
  - → An introductory meeting between the auditor and the site team.
  - → Auditor briefs the scope and procedures to be followed during the audit.
  - → An opportunity for trial team members to communicate with the auditor.

- Reviewing documents and collating information
- Audit observations (documents all observations)

□ After the audit process:

- Auditor should issue the audit report within 28 days of the final audit activity.
- He makes clinical research personnel

aware of the findings relevant to their activities, and findings are classified as critical, major and minor.

- Prevention / corrective action list should accompany the report.
- A formal audit response should be prepared and submitted by the trial team to the concerned personnel after the corrective measures have been taken.
- Following the satisfactory responses to the audit, auditor issues an audit certificate confirming that audit has taken place and filed in clinical trial report and also submitted to regulatory authorities.

Clinical Research Coordinator (CRC)

- The clinical Research Coordinator (CRC) is responsible for conducting clinical trials using Good Clinical Practice (GCP) under the auspices (يشتبان) of the Principal Investigator (PI).
- Good Clinical Practices Principles have been defined by Madelene Ohosen, RN, MSN, of The University of Texas Health Science Center at Houston as:
- All trials are conducted ethically, as defined by the Declaration of Helsinki, rigorously (بدقة), as defined by the International Conference on Harmonization Guidelines (ICH).
- Benefits outweigh risks for each patient.
- Rights, safety and well-being of patients prevail (يسود) over science.
- All available non-clinical and clinical information on any investigational agent can

Support the trial as designed.

- All trials are scientifically sound and clearly described.
- All clinical trials have current Institutional Review Board approval.
- Medical decisions and care are the responsibility of qualified health care professionals, specifically physicians and, if applicable, dentists.
- Everyone involved in the clinical trial is qualified by training, education and experience.
- Informed consent is given freely by every participant.
- All study documentation is recorded, handled and stored to allow accurate reporting, interpretation and verification.
- Confidentiality of subjects is respected

and protected.

- Investigational products maintain Good Manufacturing Practice in storage, manufacturing and handling.
- Systems to ensure quality are implemented in all aspects of the trial.

- Although the PI is responsible for the conduct of the trial, "it has been said that the CRC is the heart and soul of the research study and that, ultimately, it is the CRC who carries forward the research goals, thereby playing a significant role in the success of the research study. Most importantly, CRCs are often involved in essential duties that have been traditionally performed by the PI, such as conducting the informed consent process

and ensuring compliance with the protocol".

- The CRC's primary responsibility, as with all clinical research professionals, is the protection of human subjects, but the CRC has many other responsibilities.

- Although not inclusive, some of the CRC responsibilities include preparing the Institutional Review Board submission, writting the informed consent document, working with the institutional official in contact negotiations, developing a detailed cost analysis, negotiating the budget with the Sponsor (i.e. pharmaceutical company or granting agency), subject recruitment, patient care, adverse event reporting, preparing the case report form ("CRF), submitting CRFs and other data to the Sponsor as necessary and study close-out.

Responsibilities:

1. Institutional Review Board Submissions
2. Informed consent
   - Basic elements
   - Additional elements
3. Contracting with pharmaceutical companies
4. Cost analysis and budget negotiations
5. Subject recruitment
6. Patient care
7. Adverse events
8. Case report forms
9. Study close

1. Institutional Review Board Submissions:

All research involving human subjects must be approved by an Institutional Review Board. Each IRB has requirements for protocol submi-

ssions which usually require the preparation of an IRB application and informed consent document. A study cannot begin unless IRB approval is obtained.

2. Informed consent:

The IRB must approve the informed consent prior to study initiation and often the CRC is liaison b/w the IRB and the sponsor. The sponsor will have set requirements of the informed consent as does the IRB.

Each local IRB is responsible for the review and approval of the informed consent, but the CRC is responsible for the communication b/w the IRB and the sponsor.

• § 46.116 of the code of Federal Regulations outlines the elements of informed consent as:

•Basic elements:

1. A statement that the study involves research, an explanation of the purpose of the research and the expected duration of the subject's participation, a description of the procedures to be followed, and identification of any procedures which are experimental;

2. A description of any reasonably foreseeable risks or discomforts to the subject;

3. A description of any benefits to the subject or to others which may reasonably be expected from the research.

4. A disclosure of appropriate alternative procedures or courses of treatment, if any,

that might be advantageous to the subject;

5. A statement describing the extent, if any, to which confidentiality of records identifying the subject will be maintained;

6. For research involving more than minimal risk, an explanation as to whether any compensation and an explanation as to whether any medical treatments are available if injury occurs and, if so, what they consist of, or where further information may be obtained;

7. An explanation of whom to contact for answers to pertinent questions about the research and research subject's rights, and whom to contact in the event of a research

related injury to the subject; and

8. A statement that participation is voluntary, refusal to participate will involve no penalty or loss of benefits to which the subject is otherwise entitled, and the subject may discontinue participation at any time without penalty or loss of benefits to which the subject is otherwise entitled.

• Additional elements:

When appropriate, one or more of the following elements of information shall also be provided to each subject:

1. A statement that the particular treatment or procedure may involve risks to the subject (or to the embryo or fetus, if the subject is

or may become pregnant) which are currently
در حال حاضر
unforeseeable.
پیش بینی نشده

anticipate: انتظار داشتن

2. Anticipated circumstances under which the subject's participation may be terminated by the investigator without regard to the subject's consent;

3. Any additional costs to the subject that may result from participation in the research;

4. The consequences of a subject's decision to withdraw from the research and procedures for orderly termination of participation by the subject;

5. A statement that significant new findings

developed during the course of the research which may relate to the subject's willingness to continue participation will be provided to the subject; and

6. The approximate number of subjects involved in the study.

3. Contracting with pharmaceutical companies:

The Site conducting the clinical trial will negotiate (کنٹریکٹ کرنا) the clinical trial management (CTA) to conform to its policies and procedures.

The resolution of many contractual issues requires coordination b/w the Sponsor, the PI and the Site, which is usually the responsibility of the CRC.

The involvement of each party is essential to a successful CTA with mutually acceptable terms.

•The CTA should include terms for indemnification, confidentiality, publication, intellectual property, insurance, data safety and monitoring boards, subject injury, governing law and termination clauses.

negotiation: داوستد

4: Cost analysis and budget negotiations: گفت وگو و چانه زنی

•To develop a cost analysis, the CRC will review the protocol schema and determine which procedures are standard of care versus research. The research charges will be included in the budget along with personnel effort, site initiation costs, IRB fees throughout the life of the clinical trial, pharmacy costs, travel costs for the PI and CRC to attend Investigator meetings, equipment, dedicated fax and computer lines, supplies, screen failures, Subject Stipends, دستمزد

Subject travel costs, and any other items that are defined as a direct cost to the clinical trial.

In addition, if the clinical trial is conducted at an Academic Medical Center (AMC) there will be an indirect cost rate that will be applied to the direct costs of the study. The indirect rate is approximately 30% for pharmaceutical trials and can be upwards of 50% for federal trials, depending on the AMC's federally negotiated indirect costs rate.

5. Subject recruitment:

Prior to agreeing to conduct the clinical trial, the CRC (and the PI) will determine if they have the appropriate patient population. The CRC is responsible for subject recruitment

once the trial begins or establishing the research team that will recruit subjects. It is important that viable subject recruitment occurs beforehand as the clinical trial agreement will stipulate the number of subjects the site is required to recruit.

6. Patient Care:

- The CRC will coordinate and conduct patient care visits and assure all procedures are conducted in compliance with the protocol.

The CRC will interact with the PI to assure patient receives appropriate medical evaluation and care when needed and will alert the PI of any serious adverse events that may occur throughout the course of the study.

7. Adverse events:

An adverse event is described as "any adverse change in health or "side-effect" that occurs in a person who participates in a clinical trial while the patient is receiving the treatment (study medication, application of the study device, etc.) or within a pre-specified period of time after their treatment has been completed". The CRC must report all adverse events to the sponsor and all serious adverse events to the IRB and sponsor.

8. Case report forms:

The purpose of the case report form (CRF) is to collect relevant data in accordance with the protocol and in compliance with regulatory requirements.

The CRC will collect the data on the CRF and submit to the Sponsor either electronically or paper format.

9. Study close:

In accordance with the local IRB, the CRC will complete IRB Study close documentation and make any appropriate notifications to the Study Subjects, research team, and pharmacies.

- The CRC will work with the Sponsor's clinical monitor in completing outstanding monitoring findings and queries.

In addition, the CRC is responsible for complying with the record retention policies of the FDA, the ICH, and the clinical trial agreement.

authority: (اتھارٹی/اختیار)

Introduction:

- National regulatory authorities oversee (نگرانی کرنا) and monitor the development of new drugs.

1. In USA FDA oversees new drug development
2. In Europe European Agency for the Evaluation of Medicinal products (EAEM)
3. In Japan the Ministry of Health, Labour and Welfare
4. In China the State Drug Administration (SDA)
5. In India DCGI, CDSCO, SLA, NPAC, CDA

Objective:

The overall objective of a Drug Regulatory Authority (DRA) is to ensure that:

1. Medicinal products are of acceptable quality, safety and efficacy.

2. Manufactured and distributed in ways which ensure their quality until they reach the patient/consumer, and their commercial promotion is accurate.

Regulatory Authority

Roles and Responsibilities:

1. Regulatory affairs officers ensure the appropriate licensing, marketing and legal compliance of pharmaceutical and medical products in order to control the safety and efficacy of products

2. They combine their knowledge of scientific, legal and business issues to ensure products, which are developed, manufactured or distributed by a wide range of companies, meet the required legislation.

3. They advise on and coordinate the approval and registration of pharmaceuticals, veterinary medicines, complementary medicines, chemicals, pesticides, therapeutic devices and other products.

4. Regulatory affairs officers are the crucial link b/w their company, its products and regulatory authorities.

Responsibilities:

1. Ensuring that a company's products comply with the regulations.

2. keeping abreast (همسو) of international legislation (قانون), guidelines and customer practices.

Collate: (هنا بالو تطبيق کردن)

3. Collecting and collating a wide range of information

4. Keeping up to date with a company's product range

5. Developing and writing clear arguments (استدلال) and explarations for new product licenses and license renewals.

6. Preparing submissions of license variations and renewals to strict deadlines.

7. Monitoring ant setting timelines for license

variations and renewal approvals

8. Working with specialist computer software and resources

9. Writing clear, accessible product labels and patient information leaflets

10. planning and developing product trials and interpreting trial data.

11. Advising scientists and manufacturers on regulatory requirements

12. Roject managing teams of colleagues involved with the development of new products.

undertake: بعهده گرفتن

13. Undertaking and managing regulatory inspections

14. Reviewing company practices and providing

advice on changes to systems;

liaise: يتواصل

15. liaising with, and making presentations to, regulatory authorities

16. Negotiating with regulatory authorities for marketing authorization

17. Specifying storage, labeling and packaging requirements