



Overview of Good Clinical Practices


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Follow ICH Guidance

International **C**onference on **H**armonization
of Technical Requirements for Registration of Pharmaceuticals for Human Use



- Guidance provides unified standard
 - Assures credibility of data
 - Allows for comparability of different studies
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Preliminary Requirements

- Familiarity with basic terms and acronyms

- Here are some examples:

Case Report Form (CRF)

Institutional Review Board (IRB)

Informed Consent etc.



Study Glossary

- Know your responsibilities and how your team will interact with the other stakeholders



Guiding Principles

Ethically sound study – anticipated benefits should outweigh foreseeable risks

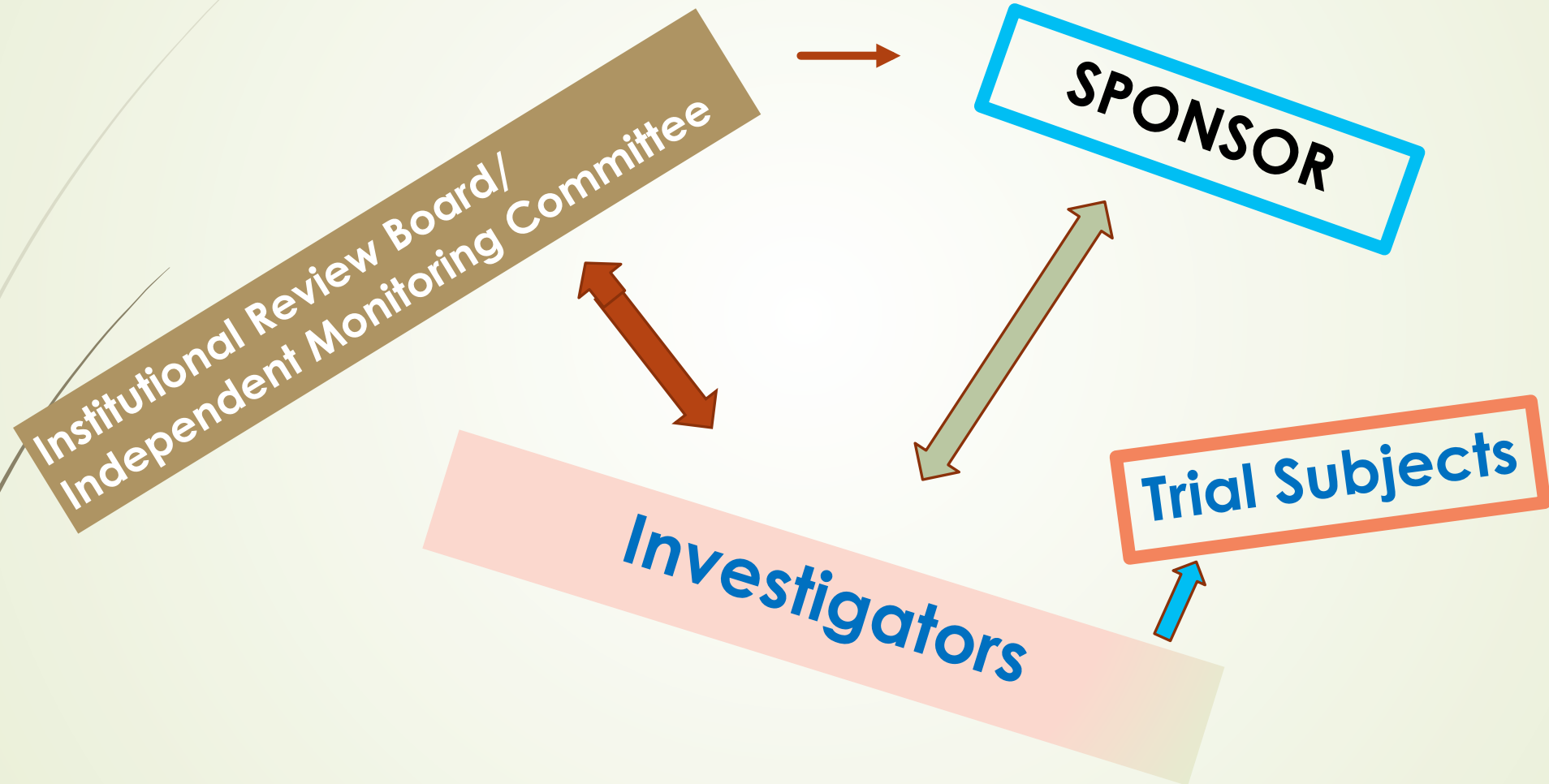
Scientific consistency and accuracy

Informed consent and protection of confidentiality

Scrupulous record keeping to ensure verification




Participants – Who's Involved





Institutional Review Board / Independent Ethics Committee

- Safeguards rights, safety & well-being of trial subjects
 - Responsible for vetting investigator qualifications and reviewing particulars of proposed trial in timely fashion
 - Can propose modifications prior to trial launch
 - Has or can have ongoing role during trial, particularly if need to amend terms or conditions of study becomes apparent
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The Investigator – *Key Competencies*

- Appropriate training and experience
- Familiarity with investigatory products and methods
- **SCRUPULOUS RECORD-KEEPING!**

*You must promptly and accurately make complete entries of all **relevant data**, such as time/date, inventories, dosages, product serial numbers, and study-specific coding of trial subjects & medications administered*

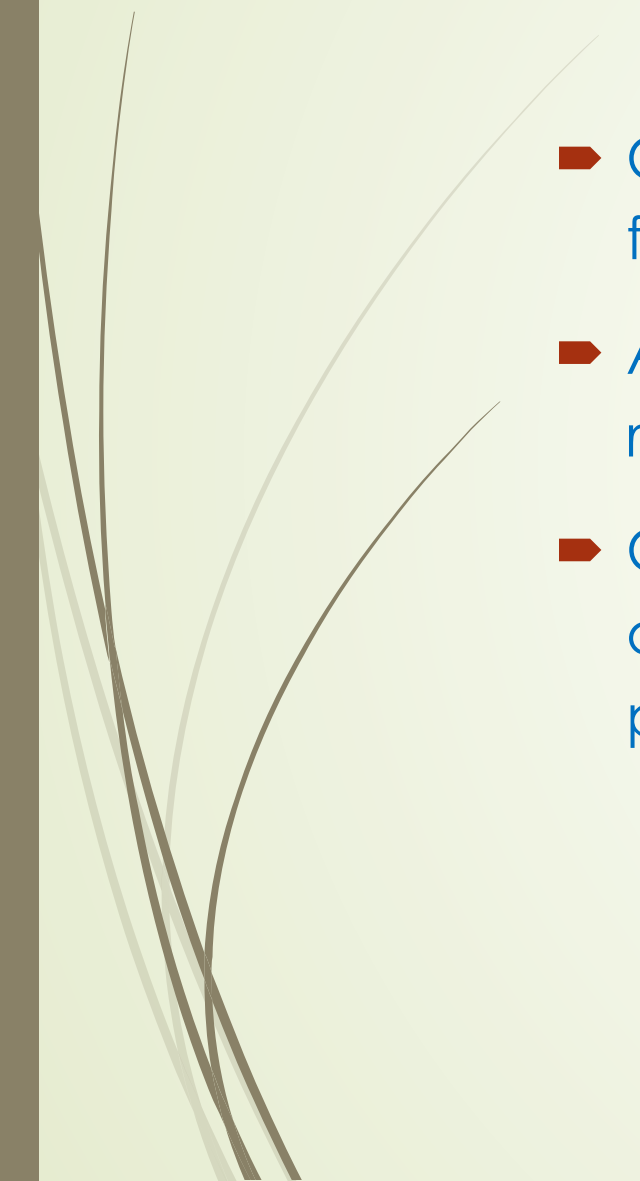


Following Protocol

- Immediate hazard is the only justifiable reason for going “off script” during trial
 - Routine compliance with study design
 - Smooth integration of ancillary resources such as pharmacy, study subjects’ medical consultations
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Personnel Interface, Stakeholder Interactions

- ▶ Clinical trial team needs adequate size and resources to function effectively
 - ▶ Anticipate interactions with study sponsor, ethics committee, regulatory agencies
 - ▶ Consistent documentation of all routine and nonroutine occurrences will facilitate communication and minimize problems
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Randomization

Is Critical

- Normally, blind or double-blind study procedures are essential for scientifically robust outcome
 - Carefully document any instances of premature unblinding, whether accidental or intentional
 - Unblinding may be just a mistake (human error)
 - Conversely, investigators may decide unblinding is necessary due to serious adverse reaction or (rarely) strong demonstration of study product's effectiveness
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Study Ethics – Informed Consent

Recruitment of subjects must follow Helsinki Declaration principles

Investigators must refrain from applying undue pressure or inducement when seeking trial subjects

Those recruited as subjects should understand the experimental nature of the study, potential risks/side effects, and relevant aspects of the protocol

A blind study means subjects could receive a placebo – understanding and accepting this possibility is especially important for informed consent in this instance



Ethics & Informed Consent (continued)

All informed consent agreements must be in writing

Revisions to standard informed consent form must receive advance approval from Institutional Review Board/Ethics Committee

Language in consent form cannot waive, or be construable as possibly waiving, trial subject's full legal rights

Investigators deal with legal representative of subjects unable to give their own informed consent; all other terms and conditions remain the same



Ethics & Informed Consent (continued)

Those being recruited as study subjects shall have opportunity to ask questions about the trial and time to consider their options

Recruited subjects should fully understand and accept

- ▶ The compensation (payment) offered for trial participation
- ▶ Terms for covering their expenses
- ▶ Medical care availability during the study
- ▶ Contingencies for redressing study-caused harm if this occurs

Just as subjects do not waive their legal rights, investigators are not absolved of legal liability for offenses such as malfeasance or fraud



During the Study . . .

- Submit regular progress reports
- Monitor and document safety

Another reminder:
Consistently accurate, regular record-keeping is
crucial!



The Clinical Trial Sponsor

- Responsible for assuring and implementing quality control
- Sponsor may transfer operation of study to Contract Research Organization (CRO), but STILL RETAINS ULTIMATE RESPONSIBILITY
- Sponsor submits trial design but must utilize fully qualified professionals in its creation
 - ▶ biostatisticians, physicians, pharmacologists, etc.



Independent Data Monitoring Committee

Using an independent monitoring committee integrated into the study process is optional, but enhanced verification would be likely

Increasing reliance on electronic data and data processing increases the need for technical consultants




But --

Monitoring committees, consultants, tech support and other entities attached to a study DON'T change who's in charge:

The SPONSOR is responsible for the trial



Sponsor – *Key Responsibilities*

- The sponsor must keep full record of all protocols, transactions, changes to the study and monitoring requirements
 - There must be clear chain of command and assignment of duties, especially if multiple outside parties have contract roles in conducting the trial
 - Both during approval process and during the actual trial, sponsor must maintain full and clear communication with relevant regulatory authority
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Adverse Incident Reporting


Safety importance makes **timely** reporting of adverse incidents crucial, to both study principals and regulatory authorities

As a corollary, possible occurrence of adverse incidents underlines how essential it is

- ▶ to have a **COMPREHENSIVE** monitoring scheme, and
- ▶ to **COMPLY** with it




Audits

- ▶ Separate from monitoring
 - ▶ Sponsor may, electively or upon request, submit audit of trial to regulatory authority to verify compliance or as added quality assurance
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Statistical Considerations

- ▶ Trial plan should include full description of statistical methodology used
 - ▶ Determine level of significance in advance
 - ▶ Sample size positively correlates with statistical power of results, and this fact encourages use of multicenter studies
 - ▶ However, use of multicenter studies poses potential commensurability difficulties
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Conclusion

- ▶ Sound study design and adherence to protocol make conducting clinical trials a thoroughly routine process in most circumstances
 - ▶ Follow ethical practices in recruiting subjects and administering the trial
 - ▶ Keep accurate records
 - ▶ Open communication will expedite uneventful studies and facilitate a more effective response to unexpected events
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