Clinical Trial Insurance

Program for the NDA Stakeholder Meeting 27th March 2019

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Presentation Outline

1. Definition of clinical trials
2. GCP and International guidelines
3. Principles of research ethics
4. Define Quality & why quality in research
5. Clinical Trials Insurance- Zimbabwe experience.
6. Concept of indemnity
7. ABPI phase 1 trial insurance-UK/EU
8. Insurance policy conditions for liability
9. Investigator & sponsor responsibilities
10. Conclusion

1.12 Clinical trial/Study definition - ICH E6 R(2)

- Any investigation in human subjects intended to discover or verify the clinical, pharmacological and/or other pharmacodynamic effects of an investigational product(s), and/or to identify any adverse reactions to an investigational product(s), and/or to study absorption, distribution, metabolism, and excretion of an investigational product(s) with the object of ascertaining its safety and/or efficacy.
- The terms clinical trial and clinical study are synonymous.

Good Clinical Practice (GCP)

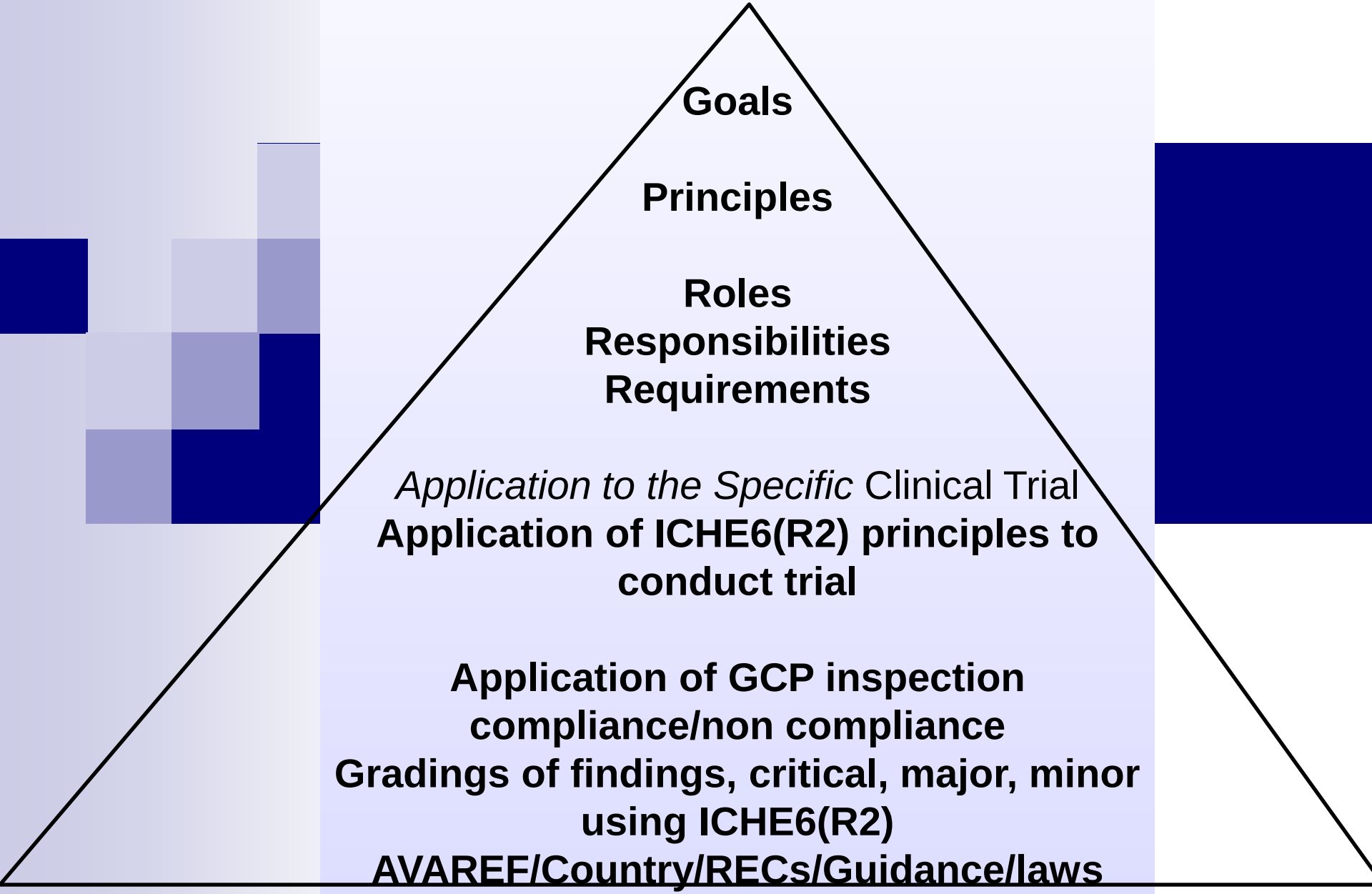
- A standard for the design, conduct, performance, monitoring, auditing, recording, analyses, and reporting of clinical trials that provides assurance that the data and reported results are credible and accurate and that the rights, integrity and confidentiality of trial subjects are protected.

What is current Good Clinical Practice(cGCP)

- cGCP is an international ethical and scientific quality standard for
  - Designing
  - Conducting
  - Recording
  - Reporting ,

  For clinical trials that involve human participants
- *Principles of current good manufacturing practice (cGMP) & current Good Laboratory Practice (cGLP) also apply.*

The Hierarchy of GCP ICHE6(R2)



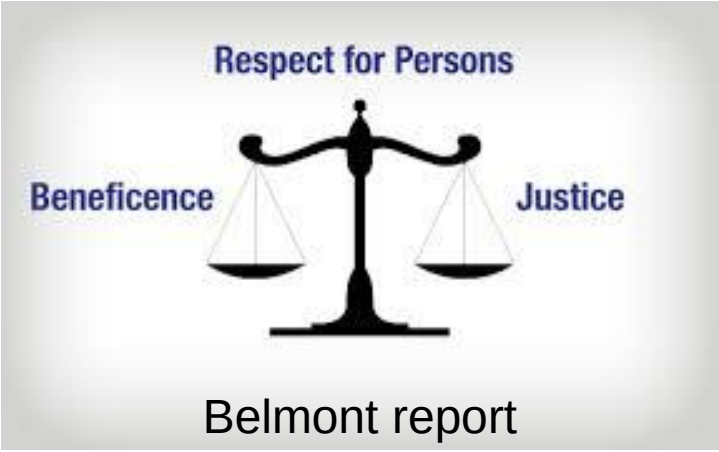
Section 1 Glossary ICHE6(R2)

- Standard definitions 65 GCP terms 1.1 to 1.65
- Standard definitions and sections 1-8 of ICHE6(R2) key for harmonization when determining the classification of clinical trial findings and GCP compliance.

International guidelines and standards

World Health Organization

CIOMS



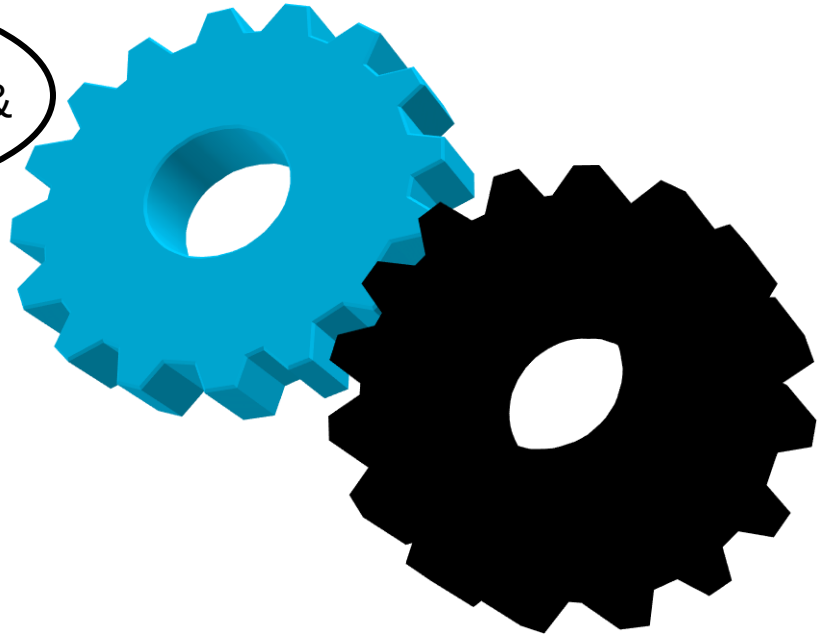
Belmont report

WMA

ICH
harmonisation for better health

Basic Principles of research on human participants

ETHICS
Protection of rights & safety



QUALITY
Credible data

Declaration of Helsinki (2013)

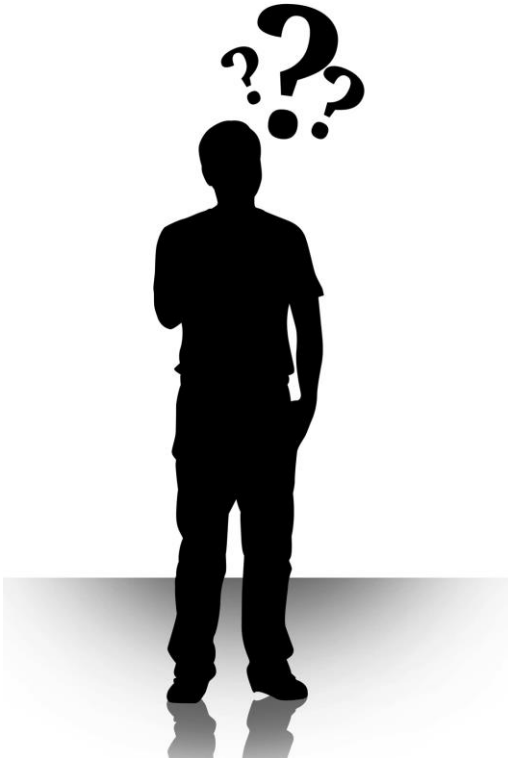
- **Guidance for research on humans, their material &/or data**
  - Safety of participants
  - Benefits > risks
  - Research protocols
  - Ethics committees
  - Informed consent
    - Vulnerable groups
  - Privacy and confidentiality

- Use of placebos
- Post-trial access to treatment
- Publishing findings and registering research
- Unproven interventions

Council for International Organizations of Medical Sciences (CIOMS)

- Facilitate and promote international activities in the field of biomedical sciences
  - International Ethical Guidelines for Health-related Research Involving Humans - 2016

Basic ethical principles in research



What are they?

Autonomy- Respect for persons

- The right for an individual to make his or her own choice
- Protection of persons with impaired or diminished autonomy, i.e. vulnerable groups
  - Informed consent – legal document for participant
  - Privacy – one ‘s right to privacy
  - Confidentiality - any and all identifiable data will be securely stored in the study site; only de-identified data will be transmitted out of the site.

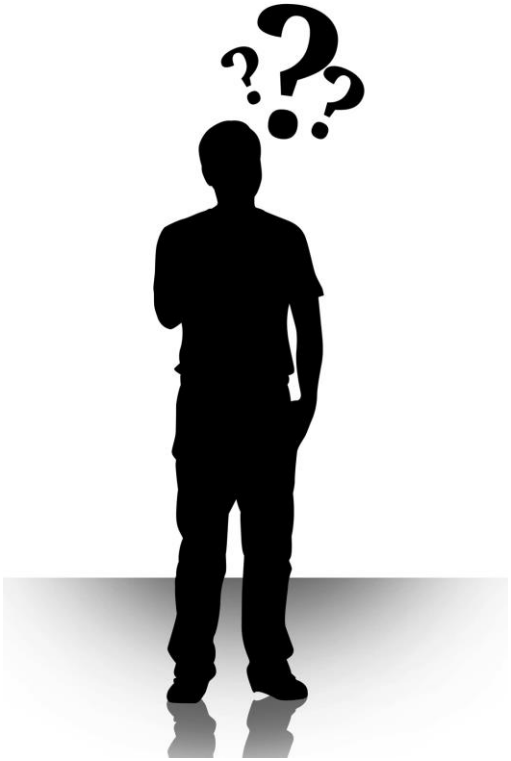
Beneficence/Non-maleficence

- The ethical obligation to
- Maximise benefits
- Minimise harms
  - Sound research design
  - Competent investigators
  - Favourable risk benefit ratio

Justice

- To treat each person according to what is morally right and proper
- Equitable distribution of both burdens and benefits of the research
    - Research be relevant and responsive to the health needs of population studied
    - Product / service developed made reasonably available

Quality in research



What do you understand by quality?

Quality

- Conformance to standards to ensure that
  - Processes are reliable (procedures are complied with)
  - Data generated are
    - Reliable (accurate)
    - Repeatable
    - Auditable (traceable)

Why data quality?

- Draw valid and meaningful conclusions;
- Comparison of data regardless of where it has been generated;
- Development of evidence based policies

How?- Scientific rigour

- Be trained on the study protocol and procedures
- Adherence to protocol, procedures & manuals
- Meticulous recording of all observations; including deviations if any
- Monitoring quality of processes and data
- Identifying non-conformances and act
  - Corrective action
  - Preventive

Quality Improvement

Improve CAPA

Act

Protocol, SOPs and training

Plan

Monitor process & data quality

Check

Do

Conducting research; collection & transmission of data

Interplay of ethics and quality

- Honesty - Truthfulness; trustworthiness of data

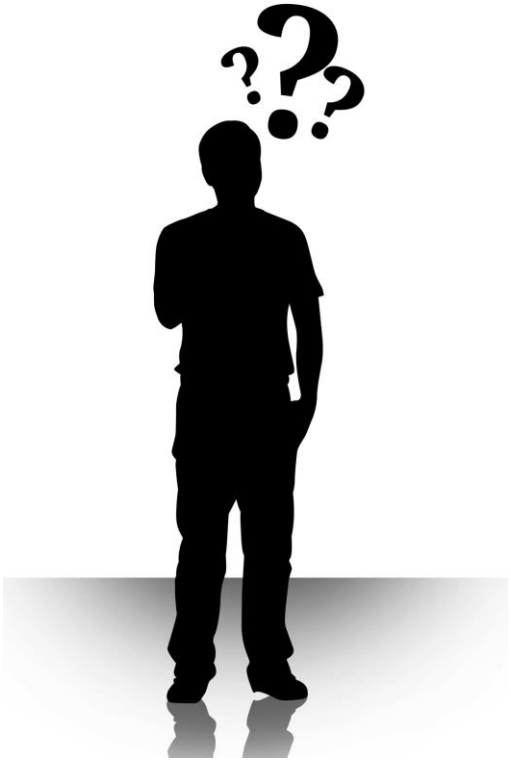
- Misconduct
- Fabrication:

  "…is making up data or results."
- Falsification:

  "…is manipulating, changing or omitting data or results such that the data is not accurately represented"

Research misconduct does not include honest error

Clinical Trial Insurance



What do you understand by clinical trial insurance?

Need for specific clinical trial insurance legislation/law

- E.g. Zimbabwe
- National Insurance Act Chapter 24 plus NRA Act
- Section 21 of the Medicines and Allied Substances Control Act [Chapter 15:03]:
- (b) insure in such amount as may be prescribed from time to time all persons or animals taking part in the trial against any injury or risk of injury that may be sustained during the trial; and

Concept of indemnity of State and NRA

- MASCA Chapter 15:03 Section 21 (c)

  sign an indemnity in such form as may be prescribed, indemnifying the State, the Secretary and the Authority from liability in respect of any injury or adverse effect whatsoever which may be sustained by any person or animal, directly or indirectly, as a result of the conduct of the trial and which occurs or reveals itself at the time of the trial or subsequently.

- Researcher signs indemnity form before conduct of study.

Concept of indemnity of Investigator/ research staff

- Country specific requirements
- Sponsor signs indemnity form before conduct of study indemnifying investigator/study staff
- Concept of HCW local insurance cover

Is there a specific designated amount that must be budgeted for research related injury?

- Yes amount calculated based on risk of study
- E.g. phase I trials highest risk
- Definition of levels of risk required and calculation formula ?
- Please Note: In 1991, USD: ZWD was about 1: 5 thus ZWD 100 000 was equivalent to USD 20 000.[3]
- The specific amount allocated in 1991 was amounting to a sum not less than ZWD 100 000 or as such as the Authority directs

Zimbabwe example CT insurance amount regulations

- Section 46 of the Medicines and Allied Substances Control (General) Regulations, 1991. S. I. 150 of 1991.
- For the purposes of paragraph (b) of section 21 of the Act, a person conducting a clinical trial shall insure the persons or animals participating in such trial for the sum of not less than one hundred thousand dollars in respect of each person or animal or such other amount as the Authority may direct.

Amendment 2019 :For the purposes of paragraph (*b*) of section 21 of the Act, a person conducting a clinical trial shall insure the persons or animals participating in such trial for the sum of –

- ~~(a)~~ **not less than one thousand United States dollars in respect of each person**
- or such other amount as the Authority may direct depending on the risk profile of the clinical trial.
- ***Indemnity forms***
- 47. An indemnity form required to be signed by an applicant in terms of paragraph (*c*) of section 21 of the Act shall be in **Form MC 20**.

Insurance and compensation in the event of injury in Phase I clinical trials Guidance by Association of British Pharmaceutical Industry (ABPI)

- Provides recommendations on level of insurance cover for phase 1 studies
- Insurance related issues and how to claim for compensation in line with UK laws and EU laws
- Legal framework, indemnity
- Limits of indemnity and other aspects of insurance cover
- Role of ECs & NRAs in determining level of compensation.
- Phase 1 studies highest risk- “First into man studies” in healthy volunteers
- UK, MAH Obligation to compensate based on ethical grounds where legal liability cannot be established
- Concept of insurance or an indemnity by third party

Insurance policy conditions for liability

- Absence of intentional misconduct on the part of the insured;
- Meeting the regulatory requirement that the study be authorised by the competent authorities;
- Making proper disclosure of background facts of the proposed study that would be material to the insurer's willingness to accept the risk or his setting of the premium;
- Making timely notification of a claim to the insurer and not compromising it without the agreement of the insurer.

Investigator/sponsor responsibilities

- Section 8 of ICHE6 R (2)
- Include among other things participants safety
- Management of Serious Adverse Events (SAEs) & reporting
- Other requirements laws/regulations
- Insurance for investigator negligence
- Sponsor insurance policy/ certificate of insurance or
- Declaration of insurance.

Other considerations

- Arbitration required if controversial claim
- Insurance is generally written on a “claims made” basis, i.e. the claim must be made in the policy period during which the insurance is in force.
- Usually within study period, to 3 years
- What happens to post trial injuries?
- Insurance cover for phase 1 sites for negligence in respect of employees/sub-contractors
- Professional liability insurance

Conclusion

- Challenges observed in implementing clinical trial insurance are usually country specific.
- Most High Income Countries have robust insurance systems in place.
- Engagement of all stakeholders key
- Comprehensive legislation/laws key
- Distinction of insurance versus compensation versus trial related injuries complex
- Consider published cases
- Participations rights, safety and protection to prevail always !

Asante
Merci
Obrigada
Thank you