Research Ethics and GCP

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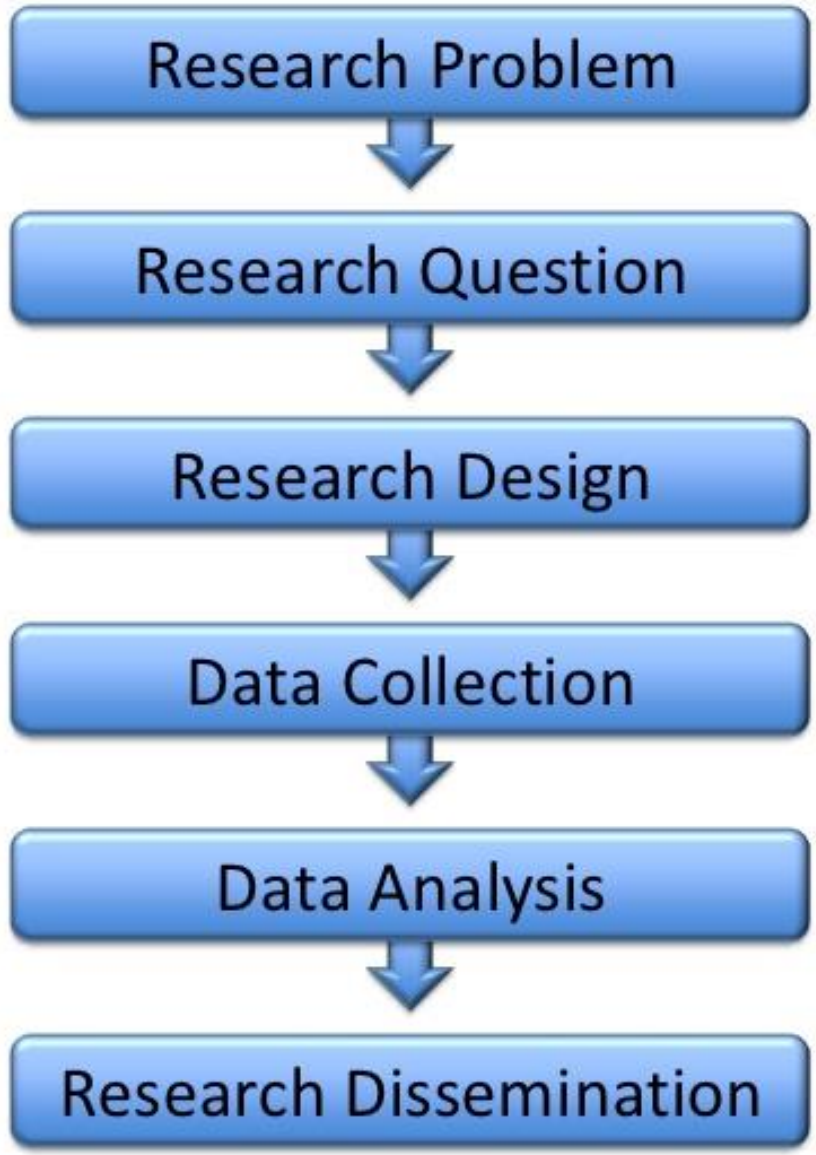
Research Ethics.....

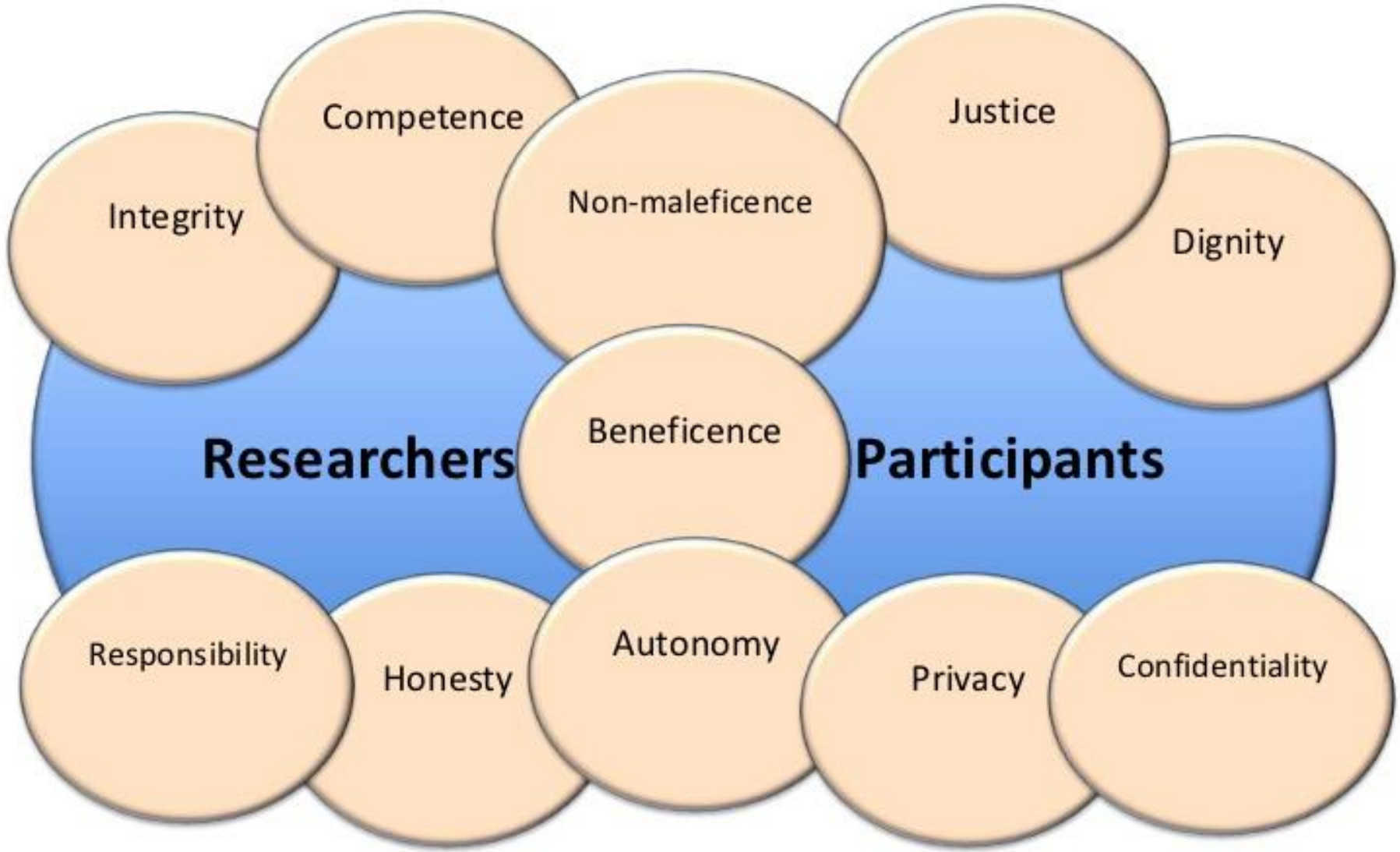
- Involves the application of fundamental ethical principles to planning, conducting & publishing of research

Guiding principles

- **Autonomy and respect**
- **Beneficence**
- **Non-maleficence**
- **Justice (free from exploitation)**
- **Scientific validity**
- **Honesty**

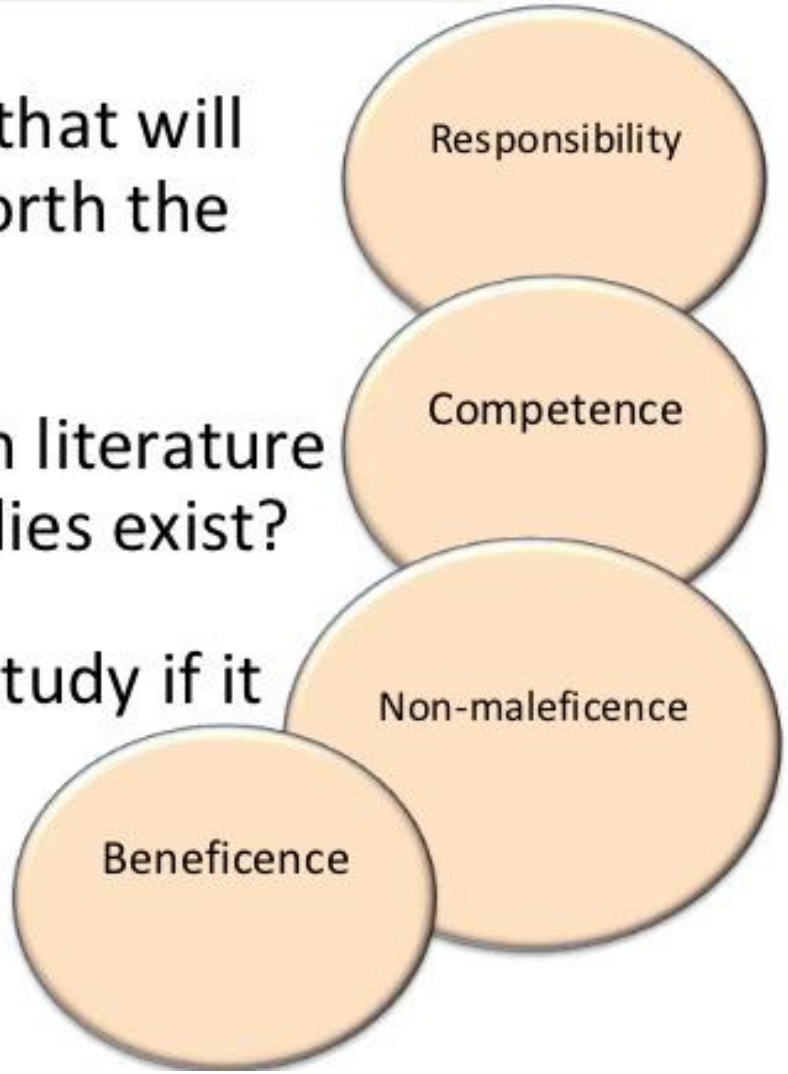

Research Problem
Research Question
Research Design
Data Collection
Data Analysis
Research Dissemination

Ethical Principles of Research



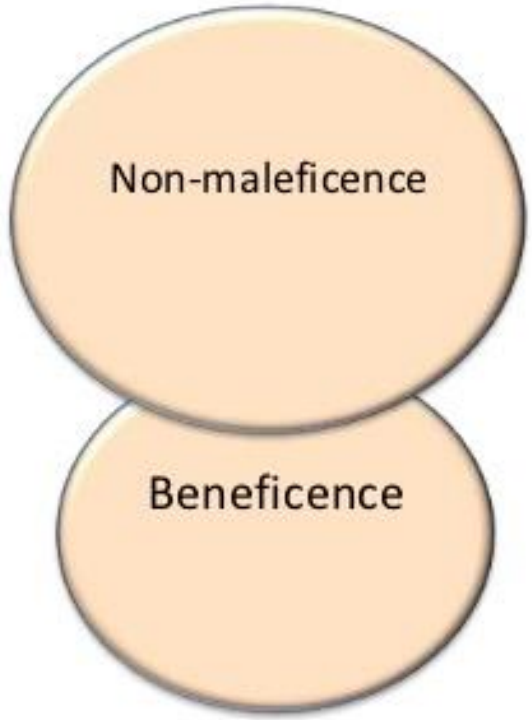
Research Problem

- Is it a significant problem that will benefit others? Does it worth the public money?
- Have you done a thorough literature review to see if other studies exist?
- Is it ethical to repeat the study if it has been done before?
  - Confirming
  - Extending
  - Refuting



Research Question

- Does it expose the participants to unacceptable risks or invasion of privacy?
- Clearly identify the purpose of the study to participants



What study needs ethics approval?

www.pre.ethics.gc.ca

- Whether the information is collected directly from subjects or from existing records not in the public domain;
- Whether the research is to be published or not;
- Whether the focus of the research is the subject;
- Whether the research is observational, experimental, correlational or descriptive;
- Whether a similar project has been approved elsewhere or not;
- Whether the research is a pilot study or a fully developed project;
- Whether the research is to acquire basic or applied knowledge; and
- Whether the research is primarily for teaching or training purposes or whether the primary purpose is the acquisition of knowledge.

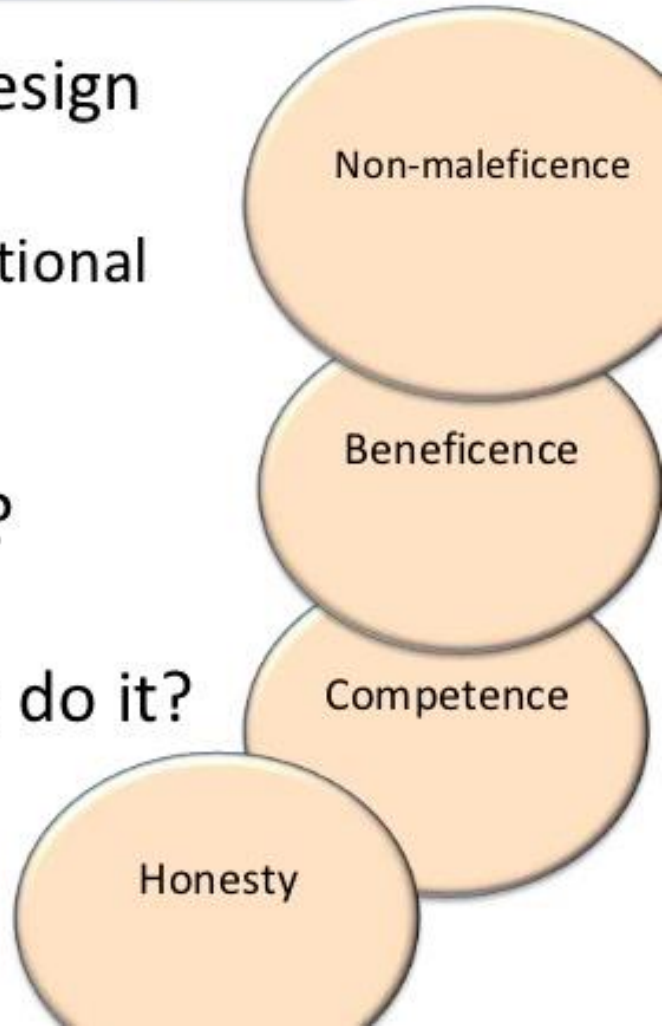
If in doubt.....

Check it out

Check with your institutional ethics review board (IRB)

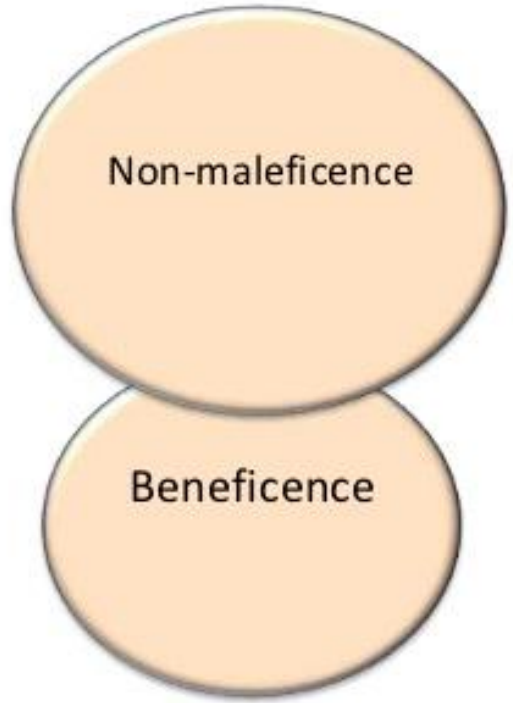
Research Design

- Is your choice of the study design an ethical choice?
  - Observational versus Interventional
  - Benefits/Risks ratio
- Is it methodologically sound?
- Do you have the expertise to do it?
  - ? Pilot



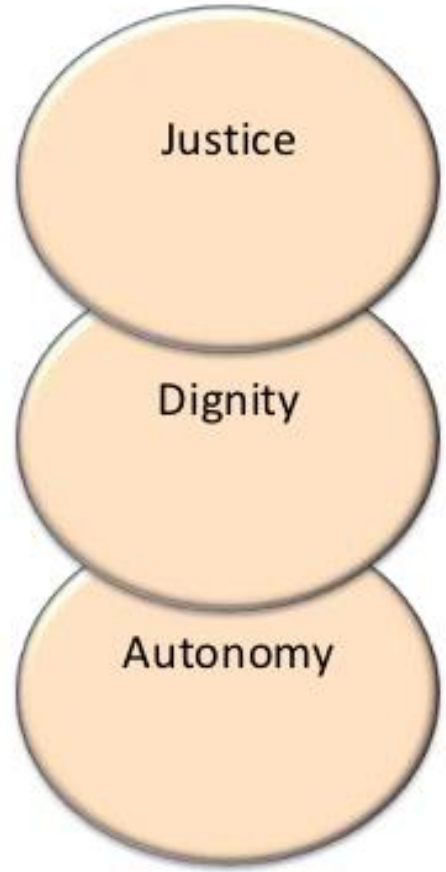
Types of Possible Harm

- Physical
- Psychological
- Social
- Economic
- Legal



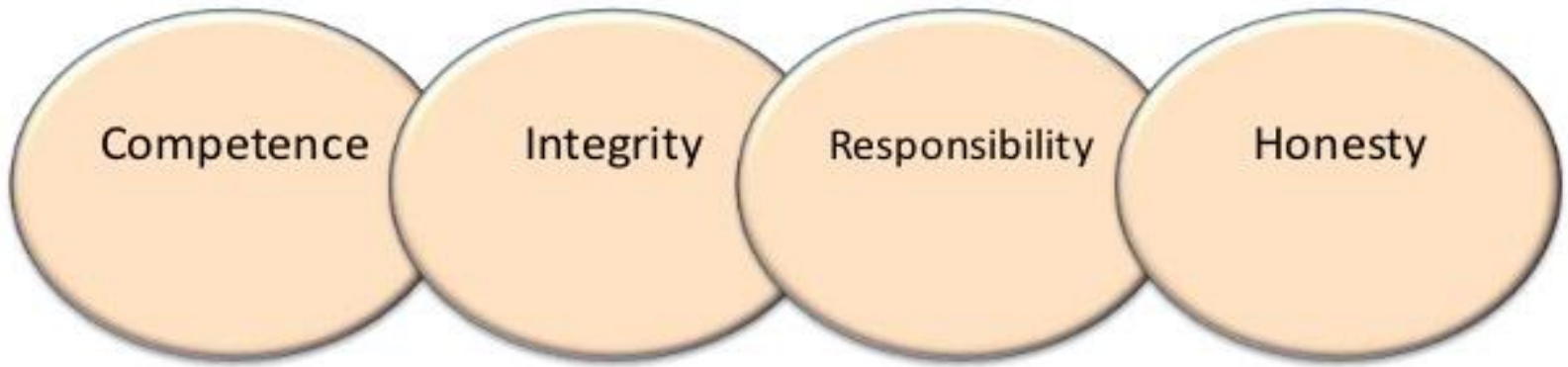
Vulnerable Populations

- Minors
- Minority groups
- Mentally incompetent
- Prisoners
- Individuals with AIDS



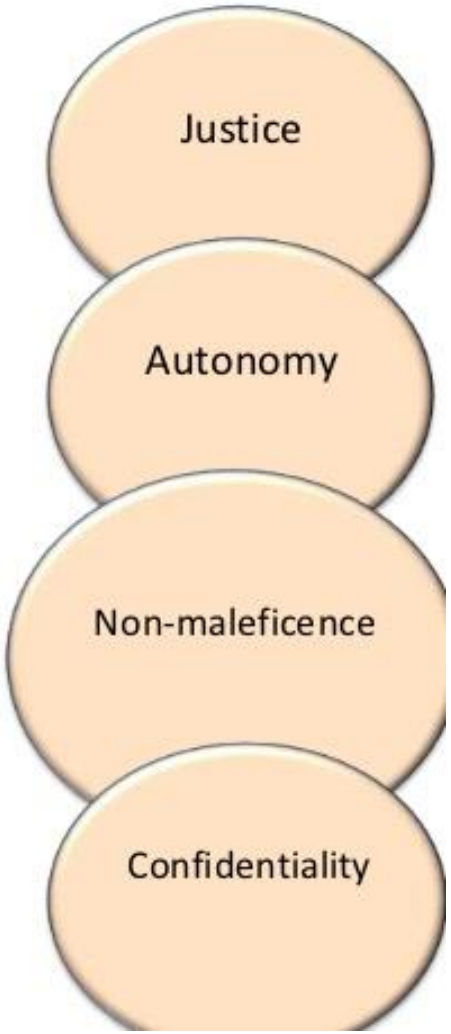
Informed Consent

- **About you & the research:**
  - Who are the researchers & their contact information?
  - Who is sponsoring?
  - What is the purpose of the research?



Informed Consent

- **About the participants:**
  - How were they selected?
  - Assurance that:
    - Their participation is voluntary
    - They can withdraw at any time
  - What are the benefits & risks for them?
  - What is the level and type of their involvement?
  - How will you ensure their confidentiality?



Data Collection

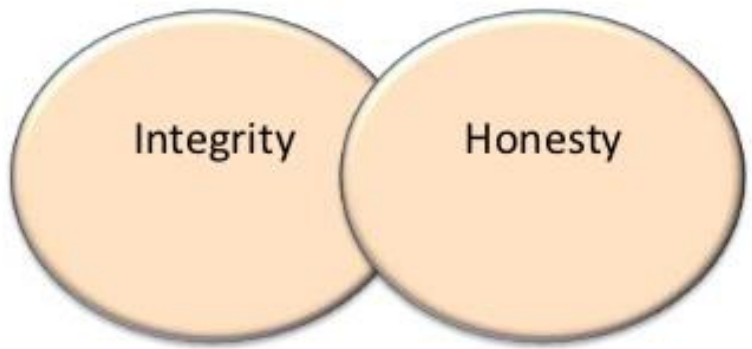
- Respect participants & research sites
- Respect privacy & confidentiality
- MONITOR

Data Analysis

- How will you protect the anonymity of participants?
- How will you analyze the data? Do you have the experience?
- How long will you keep the data once analyzed? Where & how will you keep it?

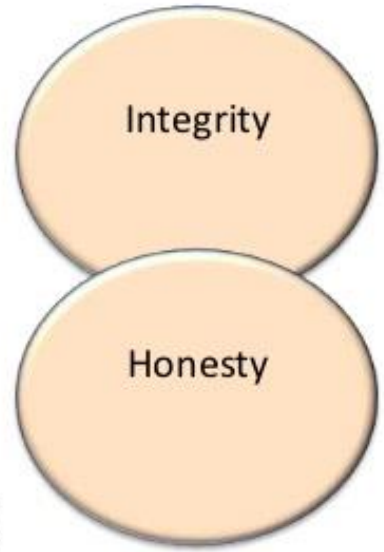
Research Dissemination

- Authorship:
  - Who will do what & when?
  - Authorship order
  - Conflicts of interests: financial



Research Dissemination

- Reporting:
  - –Fabrication
  - –Falsification
  - –Plagiarism:
    - Copying without citing
    - Paraphrasing without citing
    - Using other's ideas without citing



GCP

- Good Clinical Practice (GCP) is an international ethical and scientific quality standard for the design, conduct, performance, monitoring, auditing, recording, analyses and reporting of clinical trials
- GCP provides assurance that the data and reported results are credible and accurate, and that the rights, integrity and confidentiality of trial subjects are respected and protected . It was finalized in 1996 and became effective in 1997.
- Compliance with GCP is now a legal obligation in the UK/Europe for all trials involving the investigation of medicinal products

Historical background of GCP

- 460BC Oath of Hippocrates
- 1930's U.S. Food, Drugs and Cosmetic Act
- 1947 Nuremberg Code
- Dec 10th 1948 Declaration of Human Rights
- 1962 Kefauver-Harris Amendment
- 1964, revised 2000 Declaration of Helsinki
- 1979 The Belmont Report
- 1982 International Guidelines for Biomedical Research Involving Human Subjects
- 1996 ICH-GCP guidelines issued
- 1997 ICH-GCP guidelines becomes law in some countries

US food, drug and cosmetic act

- This was a result of harmful and lethal drugs that could be bought across the counter just like any other consumer product
- Some examples are ‘Grandma’s Secret’ and ‘Kopp’s Baby’s Friend’ which contained large doses of morphine
- In 1938, the Federal Food, Drug and Cosmetic Act was enacted by the Food and Drug Administration (FDA) and for the first time, manufacturers were required to test drugs for safety and present the evidence of safety testing to the FDA prior to marketing.

Nuremberg code

- In 1947, the Nuremberg Code was created as a result of the unethical and horrific experiments carried out during World War II at Nazi war camps by German physicians.
- This code states the need for a scientific basis in research on human subjects and voluntary consent and protection of participants

Declaration of Human rights

- The Universal Declaration of Human Rights (December 10th 1948) was also adopted and proclaimed by the United Nations after the atrocities of World War II and it further reiterated the human factor involved in medical experiments.

Kefauver-Harris Amendment

- In response to events (severe foetal limb deformities linked to the use of maternal thalidomide) the Kefauver- Harris Amendments were passed which required the FDA to evaluate all new drugs for safety and efficacy

Helsinki declaration

- In 1964, the Declaration of Helsinki was developed by the World Medical Association, forming the basis for the ethical principles that underlie the ICH-GCP guidelines we have today.
- The focus of this declaration is the protection of the rights of human subjects.

Belmont Report

- Another important milestone in the formation of the ICH-GCP guidelines
- issued in April 1979 by the National Commission for Protection of Human Subjects of Biomedical and Behavioural Research
- Principles of this report
  - Respect for person
  - Beneficence
  - Justices

- In 1982, the World Health Organization (WHO) and the Council for International Organizations of Medical Sciences (CIOMS) issued a document entitled ‘International Guidelines for Biomedical Research Involving Human Subjects

- This document was released to help developing countries apply the principles of the Declaration of Helsinki and the Nuremberg Code

- Worldwide, many organisations and committees issued various documents and guidelines on the same issue, and a decision was taken to consolidate all these guidelines into one universal guideline to be used globally

- In an effort to overcome international GCP inconsistencies throughout the countries, the International Conference for Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) issued the ICH Guidelines:

- Topic E6 Guideline for GCP.

- This guideline was approved on 17 July 1996 and

- Implemented for clinical trials from 17 January 1997.

Reasons for GCP

- Increased Ethical Awareness
- Improved Trial Methods
- Clinical Trial Concept Better Understood
- Public/Political Concern over Safety Aspects
- Frauds and Accidents during Trials
- Growing Research and Development Costs
- Increasing Competition
- Mutual Recognition of Data
- New Market Structure

13 core principles of ICH GCP

- Clinical trials should be conducted in accordance with ethical principles that have their origin in the Declaration of Helsinki, and that are consistent with GCP and the applicable regulatory requirement(s).
- Before a trial is initiated, foreseeable risks and inconveniences should be weighed against anticipated benefit for the individual trial subject and society. A trial should be initiated and continued only if the anticipated benefits justify the risks.
- The rights, safety and well-being of the trial subjects are the most important considerations and should prevail over interest of science and society.

- The available non-clinical and clinical information on an investigational product should be adequate to support the proposed clinical trial.
- Clinical trials should be scientifically sound, and described in clear, detailed protocol.
- A trial should be conducted in compliance with the protocol that has received prior institutional review board (IRB)/ independent ethics committee (IEC) approval/favourable opinion.
- The medical care given to, and medical decisions made on behalf of subjects should always be the responsibility of a qualified physician or, when appropriate, of a qualified dentist
- Each individual involved in conducting a trial should be qualified by education, training, and experience to perform his or her respective task(s).
- Freely given informed consent should be obtained from every subject prior to clinical trial participation.
- All clinical trial information should be recorded, handled, and stored in a way that allows its accurate reporting, interpretation and verification

- The confidentiality of records that could identify subjects should be protected, respecting the privacy and confidentiality rules in accordance with the applicable regulatory requirement(s).
- Investigational products should be manufactured, handled and stored in accordance with applicable Good Manufacturing Practice (GMP). They should be used in accordance with the approved protocol.
- Systems with procedures that assure the quality of every aspect of the trial should be implemented.
- These principles are self-explanatory and, when summarised, simply mean: as follows

- All clinical trials should be conducted in accordance with ethical principles, sound scientific evidence and clear detailed protocols. The benefits of conducting trials should outweigh the risks. The rights, safety and wellbeing of trial participants are of paramount importance and these should be preserved by obtaining informed consent and maintaining confidentiality. The care must be given by appropriately qualified personnel with adequate experience. Records should be easily accessible and retrievable for accurate reporting, verification and interpretation. Investigational products should be manufactured according to Good Manufacturing Practice .

GCP participants

▪ Regulatory Authorities	▪ Review submitted clinical data and conduct inspections
▪ The sponsor	▪ Company or institution/organization which takes responsibility for initiation, management and financing of clinical trial
▪ The project monitor	▪ Usually appointed by sponsor
▪ The investigator	▪ Responsible for conduct of clinical trial at the trial site. Team leader.
▪ The pharmacist at trial location	▪ Responsible for maintenance, storage and dispensing of investigational products eg. Drugs in clinical trials
▪ Patients	▪ Human subjects
▪ Ethical review board or Committee for protection of subjects	▪ Appointed by Institution or if not available then the Authoritative Health Body in that Country will be responsible
▪ Committee to monitor large trials	▪ Overseas Sponsors eg. Drug Companies

GCP adoption in Asia pacific region

- Original ICH-GCP Guidelines 1996
- Singapore GCP 1998
- Chinese GCP 1999
- Malaysian GCP 1999, revised 2004
- Thailand 2000
- Indonesia 2001
- Myanmar?