2.1 - Origin of Clinical Trial Regulations: Canadian Perspective

Presentation to APEC Preliminary Workshop on Review of Drug Development in Clinical Trials

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Disclaimer: the information within this presentation is based on the presenter's expertise and experience, and represents the views of the presenter for the purposes of a training workshop.
Objectives

Lessons from the past and present

Basic principles

Regulatory principles
Lessons from the Past and Present

• WWII experiments
• Thalidomide disaster (early 60’s)
• Diethylstilbestrol and vaginal cancer in female offspring (1971)
• Gene therapy trials (2003)
• 20 healthy volunteers infected with tuberculosis in bioequivalence drug trial (2006)
• TGN1412: 6 healthy men in critical condition (2006)
Basic Principles

1. Human life is valued therefore, must be safeguarded

2. All are equal
Ethical Guidelines

• Declaration of Geneva – WMA, September, 1948
  – “…the health of my patient will be my first consideration”

• Universal Declaration of Human Rights – UN General Assembly, December 1948
  – “Everyone has the right to life, liberty and security of person”

• Nuremberg Code – 1949
  – “The voluntary consent of the human subject is absolutely essential”
  – “The experiment should be so designed and based on the results of animal experimentation and a knowledge of the natural history of the disease or other problem under study that the anticipated results will justify the performance of the experiment”

• Declaration of Helsinki – June, 1964
  – “…to protect the life, health, privacy, and dignity of the human subject”
Impact on Canadian Framework

- IND regulations (early 60’s)

- Canadian ethical guidelines for human research were first published in the late 1970’s

  – Has its origin in the Declaration of Helsinki

- Tri-council policy statement: Ethical Conduct for Research Involving Humans – August, 1998 (currently being updated)

- Division 5 of the Food and Drug Regulations: Drugs for Clinical Trials Involving Human Subjects – September, 2001
Biomedical Research

Clinical question → Non-clinical development

- Scientific Merit
- Protection
- Validation

Clinical trials
Regulatory Principles – New Drugs

New Drugs must undergo clinical trials to “establish the safety” and demonstrate “substantial evidence of the clinical effectiveness of the new drug for the purpose and under the conditions of use recommended” before being authorized for marketing in Canada.
Regulatory Principles – Clinical Trials (1)

- Regulations state that a sponsor may not sell or import the drug for a clinical trial if:
  - there is insufficient information to assess the risks of the drug or the trial
  - the use of the drug for the purposes of the clinical trial endangers the health of a clinical trial subject or other person
  - the clinical trial is contrary to the best interests of a clinical trial subject
  - the objectives of the clinical trial will not be achieved
Regulatory Principles – Clinical Trials (2)

- Incorporation of GCP into regulations:
  - Study described in a protocol
  - All information and data available on the drug are described in an Investigator’s Brochure
  - Qualified Investigator is a trained and experienced licensed physician or dentist
  - Informed consent must be obtained from research subjects
  - Informed Consent Form must state the risks and anticipated benefits arising to the health of clinical trial subjects
  - REB review and ongoing oversight
  - Monitoring for adverse drug reactions, and reporting of all serious, unexpected, adverse drug reactions
  - Keep accurate records for specified time frame
Summary

• Lessons learned from the past and present
• International movement for the protection of human rights and research volunteers
• Incorporation of human rights principles into regulations
• Research in humans must be conducted with the highest level of scientific and ethical standards
• There is public trust in the regulator, and as regulators, we have a duty to protect
• In moving forward: life-cycle of drug product, pharmacogenomics
## References

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