Ethics in CTs
The Role of the Regulator versus The Role of the REB

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.
Review Ethic Article

Ethics in clinical Trials and Drug Development
Pharma Focus Asia
Clinical Trials
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Introduction

- Ethical elements relative to cultural realities of different jurisdictions
- Within the context of ICH GCP
- Never a single answer
- Series of dilemmas which can lead to consensus building following debate of widely divergent opinions
Role of Ethics in CTs

• Most aspects of a trial can involve ethical decisions including; design, conduct, reporting

• In the context of National and International principles, guidelines and where applicable prescribed governance

Study Design and Conduct is critical

• Little or no probability of success to demonstrate the hypothesis it is generally unethical

Inclusion Criteria and subject selection

• Important to consider if all those to be treated will derive potential benefit from the proposed therapy.

• Also important to consider if the proposed population will be exposed to undue risks

• Generally exclusion criteria are used to increase the focus and safety of CTs

Patient Follow up

• Clear delineation between the Investigator and other treating health professionals

• Ensure data integrity
Role of Ethics in CTs

Informed Consent
- Adequate information should be imparted to subjects
- Should be fair and balanced
- Full disclosure of risk
- If there is not full disclosure the data integrity is not considered to be assured

How is it ensured that CTs are conducted in an ethical manner?

Different levels of ethical review
- Ranging from a single layer under national authority
- To decentralized multilayer review
Why do we need ethical review?

- To deal with potential conflicts of interest
- Assist with openness and full disclosure of results
- Consider the use of placebos from an ethical perspective

Issues of Governance

- In many jurisdictions Ethic review is required (mandated by regulations)
- Ethics Committees are largely self-governing
- Mostly subject to ethical guidelines without regulatory oversight
- Indirect regulation does occur via ICH GCP as a high standard to help guide many aspects of CTs
- CT inspections (including REBs) provide assurance that all provisions (including ethical ones) have been respected
Are subjects in a position to judge whether the information provided in an ICF is complete?

Health Canada - Division 5
Drugs For Clinical Trials Involving Human Subjects

Application for Authorization

C.05.005. An application by a sponsor for authorization to sell or import a drug for the purposes of a clinical trial under this Division shall be submitted to the Minister, signed and dated by the sponsor's senior medical or scientific officer in Canada and senior executive officer and shall contain the following information and documents:

(a) a copy of the protocol for the clinical trial;
(b) a copy of the statement, as it will be set out in each informed consent form, that states the risks and anticipated benefits arising to the health of clinical trial subjects as a result of their participation in the clinical trial;
Example 1 of Ethics Review Issues

- A Reviewer requested that the wording of an ICF:
  - Declaration by the subject that: “This Study has been fully explained to me”
  - This is equal to “I certify the completeness of disclosure”
  - The REB in question uses “I think I understand…”
  - FDA information sheet suggests that although not prohibited, statements like this may be inappropriate
    http://www.fda.gov/oc/ohrt/IRBs/informedconsent.html
- It was pointed out to Health Canada that the ICF review should be limited to Risk Benefit
- Agreed by senior management to leave “Ethics Review to the REBs”

Can the Informed Consent Document or Informed Consent Form (ICD/ICF) be considered as part of the Protocol?
Health Products and Food Branch

Health Canada - Division 5
Drugs For Clinical Trials Involving Human Subjects

Notification
C.05.007. If the sale or importation of a drug is authorized under this Division, the sponsor may make one or more of the following changes if the sponsor notifies the Minister in writing within 15 days after the date of the change:
(a) a change to the chemistry and manufacturing information that does not affect the quality or safety of the drug, other than a change for which an amendment is required by section C.05.008; and
(b) a change to the protocol that does not alter the risk to the health of a clinical trial subject, other than a change for which an amendment is required by section C.05.008.

Amendment
C.05.008.

2) For the purposes of subsection (1), amendments are
(a) amendments to the protocol that affect the selection, monitoring or dismissal of a clinical trial subject;
(b) amendments to the protocol that affect the evaluation of the clinical efficacy of the drug;
(c) amendments to the protocol that alter the risk to the health of a clinical trial subject;
(d) amendments to the protocol that affect the safety evaluation of the drug;
(e) amendments to the protocol that extend the duration of the clinical trial; and amendments to the chemistry and manufacturing information that may affect the safety or quality of the drug.

Example 2 of Ethics Review Issues

• An CT Notification was reviewed
  ▪ It was noted that the sponsor had deleted important safety information from the ICF.
  ▪ It was decided after a brief review and discussion with the Sponsor to correct the deficiency and resubmit the information as an amendment.

• As a result an acting manager received 14 amendments
  ▪ Turned out the error affected 14 trials!

• Confusion ensued
  ▪ The acting manager believed that the ICF was separate from the protocol
  ▪ Changes to the ICF did not qualify as an amendment