Ethics Committees in the Europe Union

5th European Summer School in Clinical Pharmacology & Therapeutics Ghent

Drs. H. Pieterse
Profess Medical Consultancy B.V.
26 August 2007
Ethics Committees

• Ethics & Ethics Framework
• ICH Functions and Responsibilities (principles & guidelines)
• Implications of EU Directive on Clinical Trials
• Implications of “GCP” commission Directive
Ethics

The discipline of describing behaviour, practices, thinking and moral values generally agreed to be acceptable to society
Ethics Framework

- Declaration of Helsinki
- GCP
- Local Law
- Ethics Committees

Ethics : Society
Ethics committees

• The Declaration of Helsinki 1964

“The design and performance of each experimental procedure involving human subjects should be clearly formulated in an experimental protocol which should be transmitted for consideration, comment and guidance to a specially appointed committee independent of the investigator and the sponsor ......”
Declaration of Helsinki

• Underpins biomedical research
• Guidance to physicians and others
• Not binding – a set of principles
‘The design and performance of each experimental procedure involving human subjects should be clearly formulated in an experimental protocol. This protocol should be submitted for consideration, comment, guidance, and where appropriate approval to a specially appointed ethical review committee which must be independent of the investigator, the sponsor or any other kind of undue influence’.

(Basic Principle 13)
Declaration of Helsinki

Revised October 2000, 52nd WMA, Edinburgh

‘This independent committee should be in conformity with the laws and regulations of the country in which the research experiment is performed. The committee has the right to monitor ongoing trials. The researcher has the obligation to provide monitoring information to the committee. The researcher should also provide to the committee for review, information regarding funding, sponsors, institutional affiliations, other potential conflicts of interest and incentives for subjects’.

(Basic Principle 13)
Declaration of Helsinki

• Issues with 2000 version
  - Placebo
  - “Best current” diagnosis and treatment
Ethics Committee

- An IRB/IEC should safeguard the rights, safety, and well-being of all trial subjects. Special attention should be paid to trials that may include vulnerable subjects.

ICH GCP 3.1.1
ICH GCP 3.1 Responsibilities

• Review proposed trial ‘within a reasonable time’ and provide written details, including:
  • Trial details
  • Documents reviewed
  • Relevant dates
  • Approvals/modifications required prior to approval
  • Disapproval/negative opinion
  • Termination/suspension of prior approvals
ICH GCP 3.1 Responsibilities

• Documents
  • Protocol + amendments
  • Investigator brochure
  • Consent form + updates
  • Patient information sheet + updates
  • Investigator's CV & qualifications
  • Recruitment procedures, including advertisements
  • Available safety information
  • Payment/compensation to subjects
  • ‘Other documents required to fulfil its responsibilities'
ICH GCP 3.1 Responsibilities

- Ongoing review; at least once a year - risk to subjects
- Non-therapeutic trials with consent of legal representatives; protocols must address ethical concerns & regulatory requirements
- Emergency recruitment (no consent); protocols must address ethical concerns & regulatory requirements
ICH GCP 3.2
Composition, functions and operations

- At least 5 members
- At least one member whose primary area of interest is in a non-scientific area
- At least one member who is independent of the institution/trial site
- A list of IEC members and their qualifications should be maintained
ICH GCP 3.2
Composition, functions and operations

- Must function according to written operating procedures and maintain written records of activities
- Make decisions at announced meetings at which at least a quorum (as stipulated in SOPs) is present
- Only members who participate in the review may vote
- Special expertise may be co-opted (but no vote if involved in trial)
ICH GCP 3.3
Documented, written procedures

- Composition (names and qualifications of members)
- Conducting initial and continuing review of trial
- Frequency of continuing review
- Expedited review/approval of minor amendments
ICH GCP 3.3.7
Protocol amendments

All protocol amendments must be approved before being implemented in a trial except:
- when necessary to eliminate immediate hazards to subjects
- when the change involves only logistical or administrative aspects of the trial
ICH GCP 3.4 Records

- Ethics Committee should retain all relevant records from the trial for at least 3 years after completion of trial
- Records must be available upon request of regulatory authorities
- Written procedures & membership lists must be available if requested by investigators, sponsors, regulatory authorities
ICH GCP 5.11
Sponsors’s confirmation of review

• - Name & address of IEC (& composition 3.4)
• - Statement regarding GCP compliance
• - Exact details of trial and documents reviewed
• - Date of review, decision/opinion with reasons
• - Procedures for appeal
CT Directive v ICH

- The Directive is not as specific as ICH about the measures necessary for establishment and operation of an IEC
- ICH does not specify any timelines for IEC review but the Directive gives very clear timelines.
CT Directive - Ethics Committees

• the MS have to take measures to establish Ethics Committees
  – single opinion per member state for multicentre trials

• to give opinion maximum 60 days from receipt of “valid” application
  – one opportunity for further information
Process for Ethics Committee

SPONSOR

Valid Application

Response to Request

Application

Max
60 days

Single Request for additional information
Timelines for Ethics Committee

- **Standard Products**: Maximum of 60 days
- **Gene therapy, Somatic cell therapy, Genetically Modified Organisms**: +30 days
- **External consultations**: +90 days
- **Xenogenic cell therapy**: No time limit
CT Directive

Article 6: the IEC shall consider:
- The relevance of the clinical trial and the trial design
- Whether the evaluation of the anticipated benefits and risks is satisfactory and conclusions justified
- The protocol
- The suitability of the investigator and supporting staff
- The investigator’s brochure
- The quality of the facilities
CT Directive

Article 6: the IEC shall consider:

- The consent form and patient information sheet
- Procedure to be followed for obtaining informed consent
- Justification for research on persons incapable of giving informed consent
- The arrangements for the recruitment of subjects
CT Directive

Article 6: the IEC shall consider:

- Provision for indemnity or compensation in the event of injury or death
- Insurance or indemnity to cover the liability of the investigator and sponsor
- The amounts and arrangements for rewarding or compensating investigators and trial subjects and the relevant aspects of any agreement between the sponsor and the site
CT Directive
Amendments:

• Substantial amendments, likely to have an impact on the safety of the trial subjects and change the interpretation of the scientific documents must be notified to regulatory authorities and ethics committees
• Ethics committees must give an opinion on the amendment within 35 days
• Amendments cannot be implemented without approval unless immediate hazard
GCP Directive (2005/ 28/ EC)

• Ethics committee requirements

In order to further harmonise the procedures the directive states:
  – Each IEC shall adopt procedures to implement EU directive 2001/20/EC
  – IEC shall retain essential documents for at least 3 years after completion of the trial (as per ICH GCP)
  – IEC and CAs shall communicate using appropriate and efficient systems
Ethics Committees

SUMMARY

• The Directive is not as specific as ICH about the measures necessary for establishment and operation of an IEC but gives very clear timelines for review

• Each MS has to take measures to establish Ethics Committees

• We all have an obligation to protect the dignity, rights, safety and well-being of research subjects
Good Clinical Practice

‘Ethics cannot be grafted onto a trial - it must be built in from the onset.

Ultimately an ethical attitude must pervade the approach to clinical investigations, its establishment and follow through’

Quote from European Directive
Stakeholders in research

• Patients and public
• Authorities
• Medical profession/ investigators and team
• Management
• Universities
• Industry
Non-compliance

More rules

Less compliance

Less motivation

Conflict of interest

Misconduct

Parties

Interest

Control

Fraud

Problems

Legal actions

Inspection

Scientific misconduct

Less patients for trials

Public trust lower
For all research activities, but also for patient care the following criteria guarantee compliance with all rules and regulations including GCP:

- Reasonable and realistic
- Valuable
- Accountable
- Credible
- Transparent
Thank you

Questions please