POSTGRADUATE COURSE 2005

ETHICAL ISSUES IN RESEARCH

- informed consent-

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Objectives of this session:

- review need for research ethics
- highlight key issues in research ethics
- focus on and analyse the issue of informed consent

Ethical Issues in Research

- Importance of ethics in research:

Funding & publishing requirements?

Ethical Issues in Research

- Importance of ethics in research:
  - Human participants
  - Risks/ benefits not always predicted
  - Harm
  - Abuses in research

Ethical Issues in Research

Nazi experiments

Nuremberg trial- Nuremberg code 1947

The emergence of ethics

Hippocrates
(5th Century BCE)

Fundamental ethical elements of the Hippocratic oath:

- maintain doctor-patient confidentiality
- do no harm (physical, psychological, social)
- practice for the benefit of the patient

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The evolution of research ethics

Moses Maimonides (1135-1204)

Instructed colleagues always to treat patients as ends in themselves, not as means for learning new truths.

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The evolution of research ethics

Roger Bacon
(1214-1294)

"The operative and practical sciences which do their work on insensate bodies can multiply their experiments until they get rid of deficiency and errors, but a physician cannot do this because of the nobility of the material in which he works; for that body demands that no error be made in operating upon it, and so experience *[of the experimental method]* is so difficult in medicine."

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The evolution of research ethics

Claude Bernard (1813-1878)

"Wrong to injure one person regardless of the benefits that might come to others."

An Introduction to the Study of Experimental Medicine (1865)

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The evolution of research ethics

Walter Reed (1851-1902): and his Yellow Fever Contract

"The undersigned understands perfectly well that in the case of the development of yellow fever in him, he endangers his life to a certain extent but it being entirely impossible for him to avoid the infection during his stay on this island he prefers to take the chance of contracting it intentionally in the belief that he will receive . . . the greatest care and most skillful medical service."

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Meanwhile ……
in 19th Century Europe!

- Many experiments were carried out in state institutions (using the poor, orphans, mentally ill)
- Experiments involved, for example, exposing subjects (and their contacts) to gonorrhea and syphilis
- In many cases, the subjects had no knowledge they were taking part in research, much less gave consent
- When the studies were reported, there was little, if any, criticism in the medical or popular press
- ***Finally***, by 1900, one government did act …….

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Prussian Prohibitions on Nonbeneficial Interventions (1900)

Directive to heads of clinics and similar establishments ***"absolutely prohibiting"*** medical interventions ***"for purposes other than diagnosis, therapy, and immunization"*** when:

1. the person in question is a minor or is not fully competent on other grounds;
2. the person concerned has not declared unequivocally that he/she consents to the intervention; or
3. the declaration has not been made on the basis of a proper explanation of the adverse consequences that may result from the intervention.

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German Regulations (1931)

Clearly distinguished between:

- *"therapeutic experimentation and modes of treatment which serve the process of healing even though the effects and consequences cannot yet be adequately determined"*

and

- *"human experimentation" (which consists of "operations and modes of treatment . . . carried out for research purposes which are not therapeutic")*

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Ethical Issues in Research

- Tuskegee syphilis experiment : 1932-1972
- Contraceptive research on poor women
- Plutonium injections

agreement about these abuses

Ethical Issues in Research

Nuremberg code
1947

Declaration of Helsinki
1964/1975/2000

CIOMS Guidelines
1982/2002

- Respect for persons
- Beneficence
- Justice

Fundamental Ethical Principles in Research

- Respect for persons
- Beneficence
- Distributive justice

Ethical Issues in Research

Respect *for persons*

↓

Respect for autonomy

CIOMS Guidelines- 2002

"For all biomedical research involving human subjects, the investigator must obtain the ***informed consent*** of the prospective subject or, in the case of an individual who is not capable of giving informed consent, the permission of a legally authorized representative in accordance with applicable law. Waiver of informed consent is to be regarded as uncommon and exceptional, and must in all cases be approved by an ethical review committee. "

Ethical Issues in Research

- Informed decision-making key issue in research involving human subjects
- International codes, guidelines,national legislation, etc.

Ethical Issues in Research

- **informed consent, and**
- **informed decision-making**

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Informed decision-making requires:

- information from the investigator to be:
  - comprehensive (complete)
  - comprehensible (simple language)

- the decision by the subject to be:
  - based on competence (ability to understand)
  - voluntary (free of coercion, undue influence or inducement, or intimidation)

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Ethical Issues in Research

- **Content** of informed consent
- **Who** obtains consent
- **How** is consent obtained
- How is consent **recorded**

THE CONSENT FORM

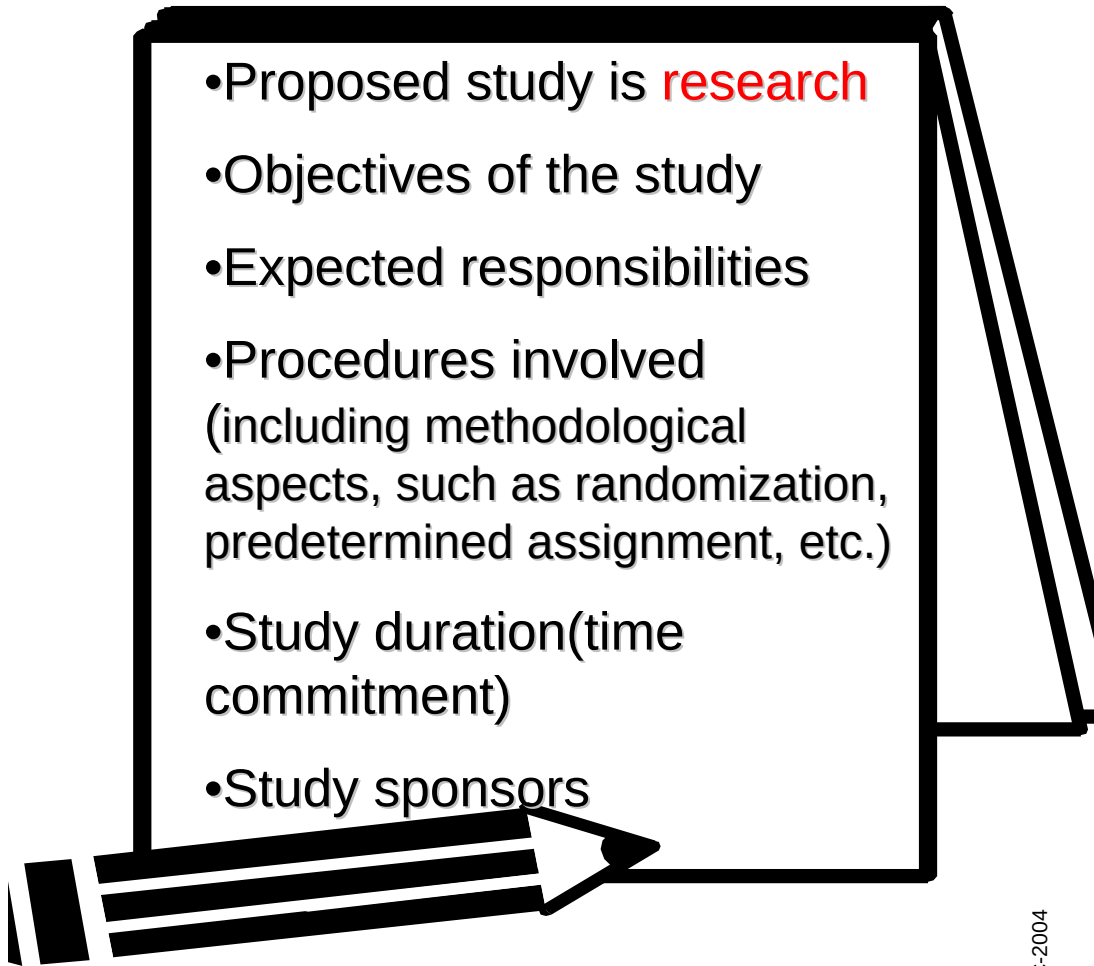
- **documents the consent process**
- **it cannot substitute for the consent information and discussion**
- **it is not to provide legal protection for researchers!**

Ethical Issues in Research

What information must be disclosed?

Ethical Issues in Research

- **Research description** ✓
- Risks
- Benefits
- Alternatives
- Confidentiality
- Compensation
- Contacts
- Voluntary participation



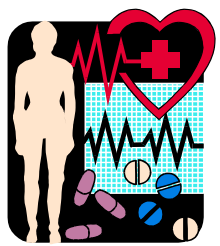
- Proposed study is research
- Objectives of the study
- Expected responsibilities
- Procedures involved (including methodological aspects, such as randomization, predetermined assignment, etc.)
- Study duration(time commitment)
- Study sponsors

Ethical Issues in Research

Points to remember:

- ***use*** **simple, nontechnical language that subjects can understand**

- **Sophisticated scientific concepts**



- **Level of literacy**

- **Cultural beliefs for disease aetiology**

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Ethical Issues in Research

Language:

Examples from US study
Waggoner , W. And Mayo D. "Who understands? A Survey of 25 Words of Phrases Commonly Used in Proposed Clinical Research Consent Forms," IRB: A Review of Human Subjects Research, vol. 17, No 1 (1995), 6-9

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Ethical Issues in Research

1. If you were to use the *barrier method* for birth control, what would this involve?

Greater than 12th grade:

a)25% **b)79%** **c)90%**

12th grade or less:

a)70% **b)35%** **c)58%**

Ethical Issues in Research

1. If you were to use the *barrier method* for birth control, what would this involve?

Greater than 12th grade:

a)25% **b)79%** **c)90%**

12th grade or less:

a)70% **b)35%** **c)58%**

2. What does the term *efficacy* mean?

Greater than 12th grade:

a)39% **b)82%** **c)59%**

12th grade or less:

a)29% **b)13%** **c)49%**

2. What does the term *efficacy* mean?

Greater than 12th grade:

a)39% **b)82%** **c)59%**

12th grade or less:

a)29% **b)13%** **c)49%**

3. If the drug you were to take was chosen *randomly*, what does this mean?

Greater than 12th grade:

a)39% **b)64%** **c)49%**

12th grade or less:

a)38% **b)13%** **c)4%**

3. If the drug you were to take was chosen *randomly*, what does this mean?

Greater than 12th grade:

a)28% **b)64%** **c)49%**

12th grade or less:

a)38% **b)13%** **c)4%**

4. What does *double-blind* mean?

Grader than 12th day:

a)65% **b)37%** **c)21%**

12th grade or less:

a)29% **b)3%** **c)17%**

4. What does *double-blind* mean?

Grader than 12th day:

a)65% **b)37%** **c)21%**

12th grade or less:

a)29% **b)3%** **c)17%**

Ethical Issues in Research

Points to remember:

- ***describe*** **fully what the subject will have to do, before, during, and following the research, including the amount of time required**
- ***include*** **mention of home visits when relevant**

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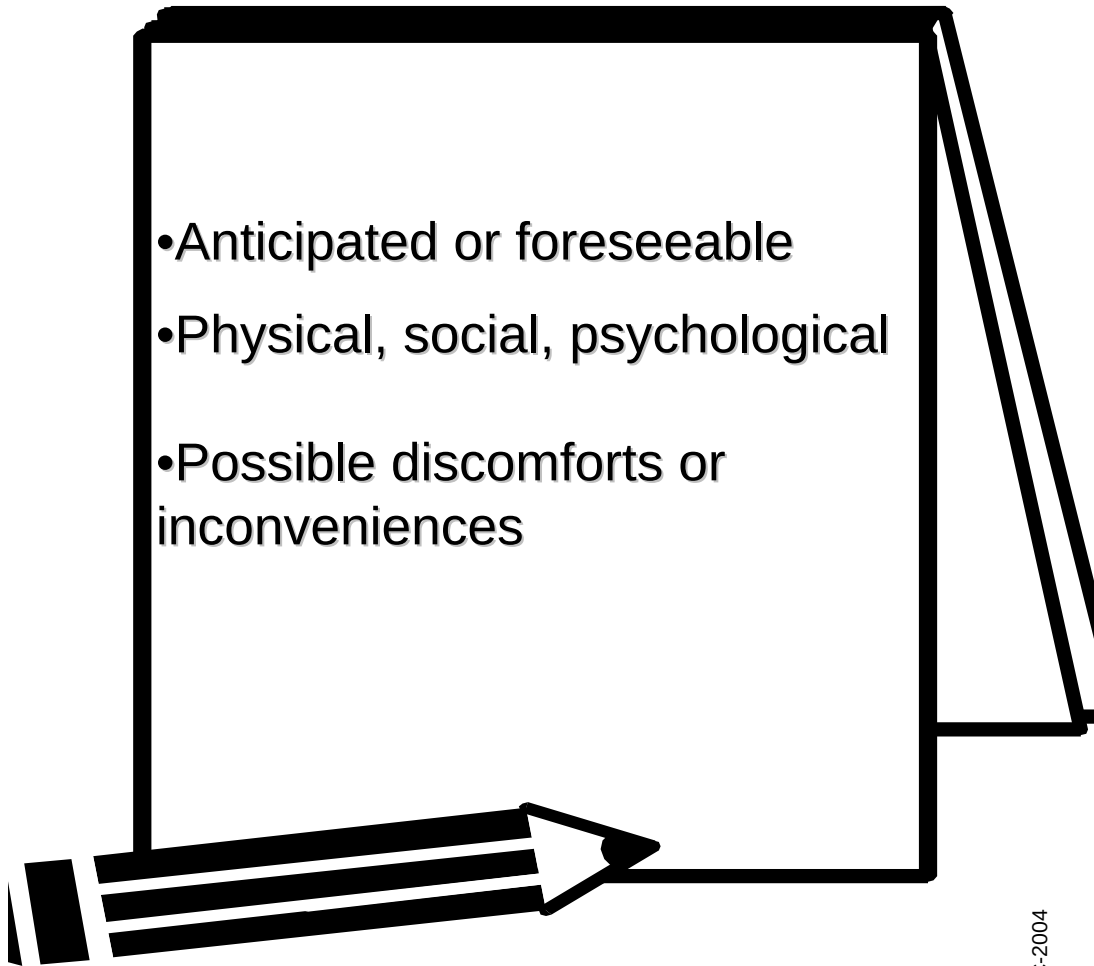
Ethical Issues in Research



Ethical Issues in Research

Points to remember:

- ***avoid*** **misleading or deceptive statements**

  e.g. "There are no risks to this research"

- ***avoid*** **unduly alarming statements**

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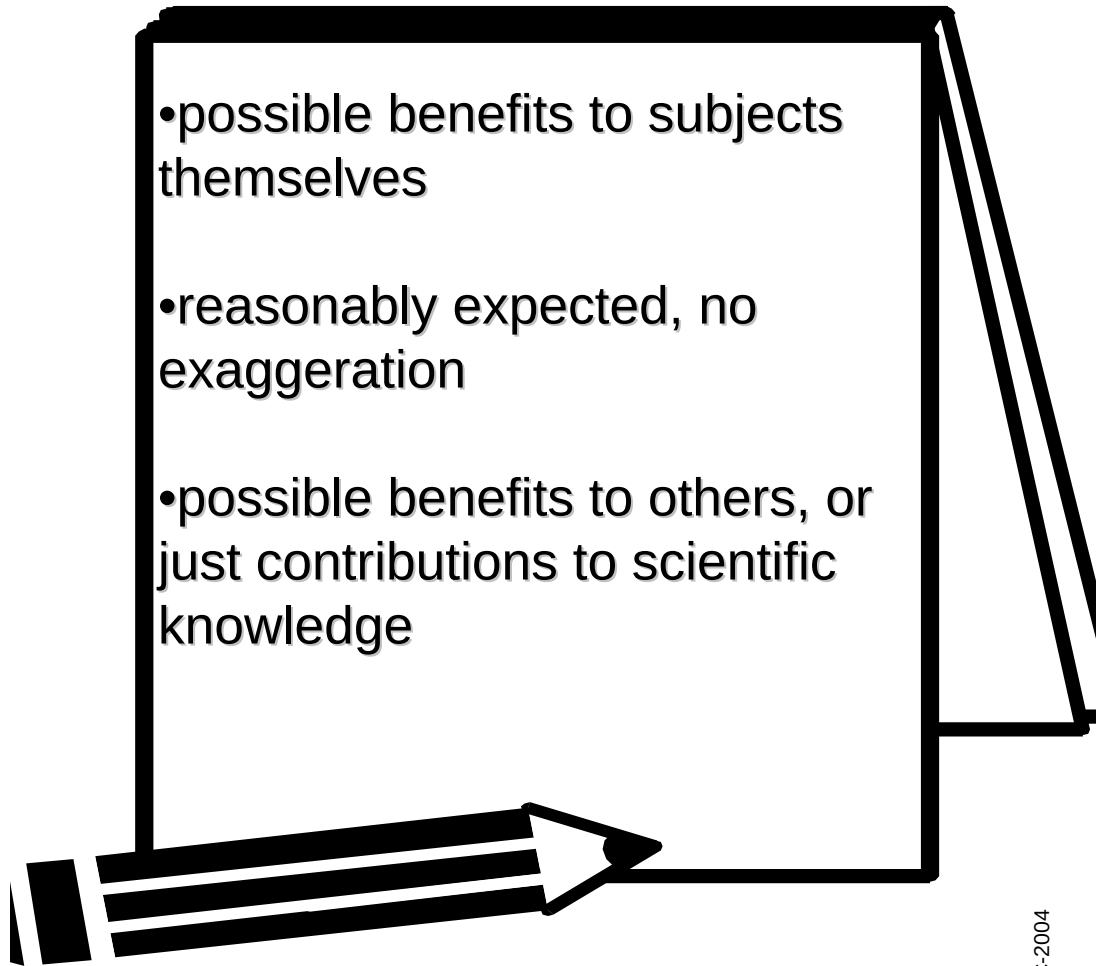
Ethical Issues in Research



Ethical Issues in Research

Points to remember:

- ***do not*** **overstate the benefits to subjects of the research**

e.g. "This new treatment will improve your condition"

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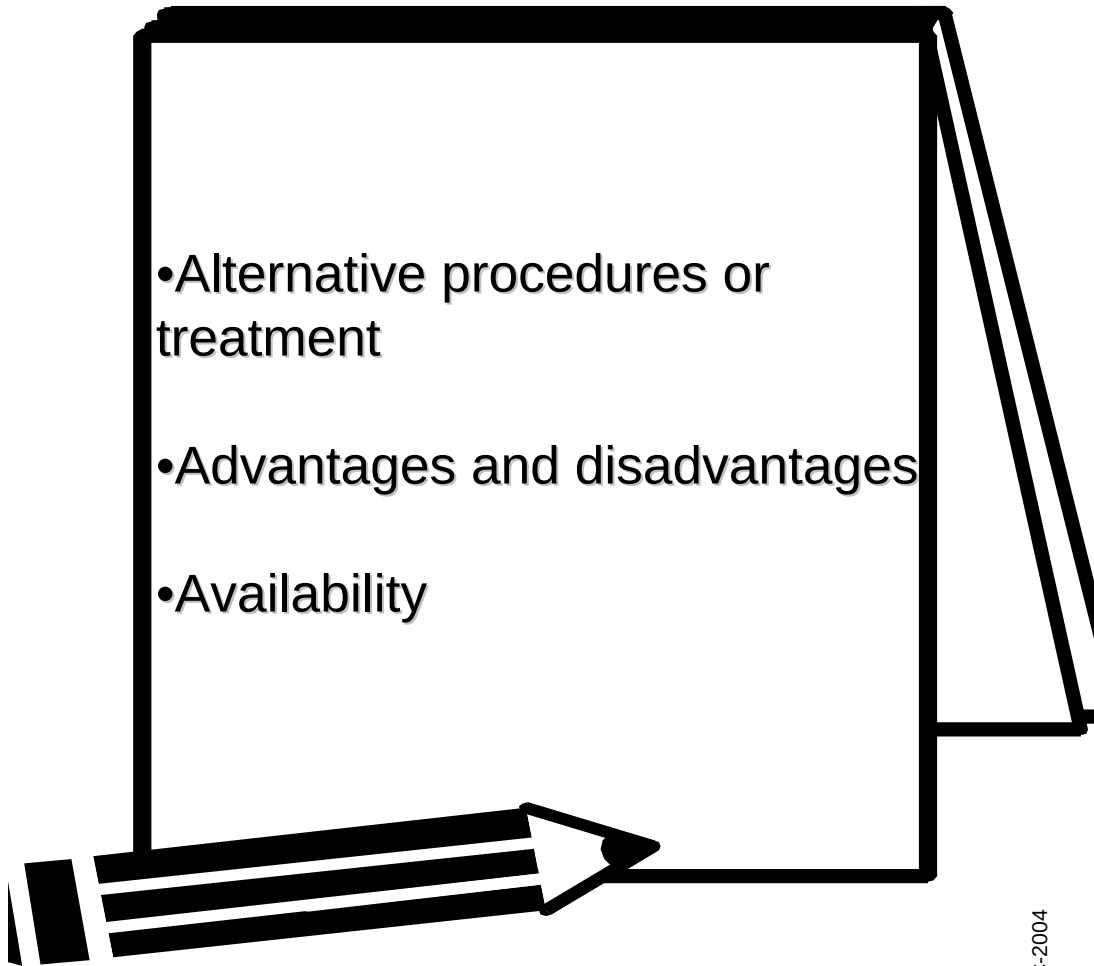
Ethical Issues in Research



Ethical Issues in Research

Points to remember:

- ***distinguish clearly*** **between the research manoeuvers and any therapeutic or diagnostic procedures subjects would undergo if not enrolled in the research**

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Ethical Issues in Research

Points to remember:

- **avoid** a ***therapeutic misconception***

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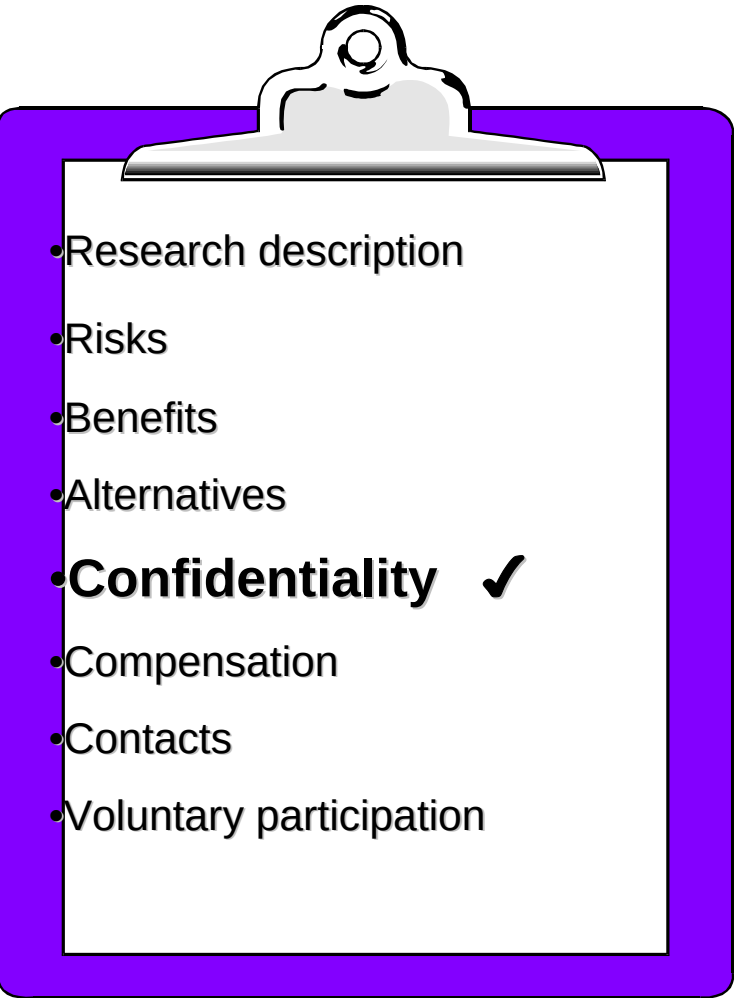
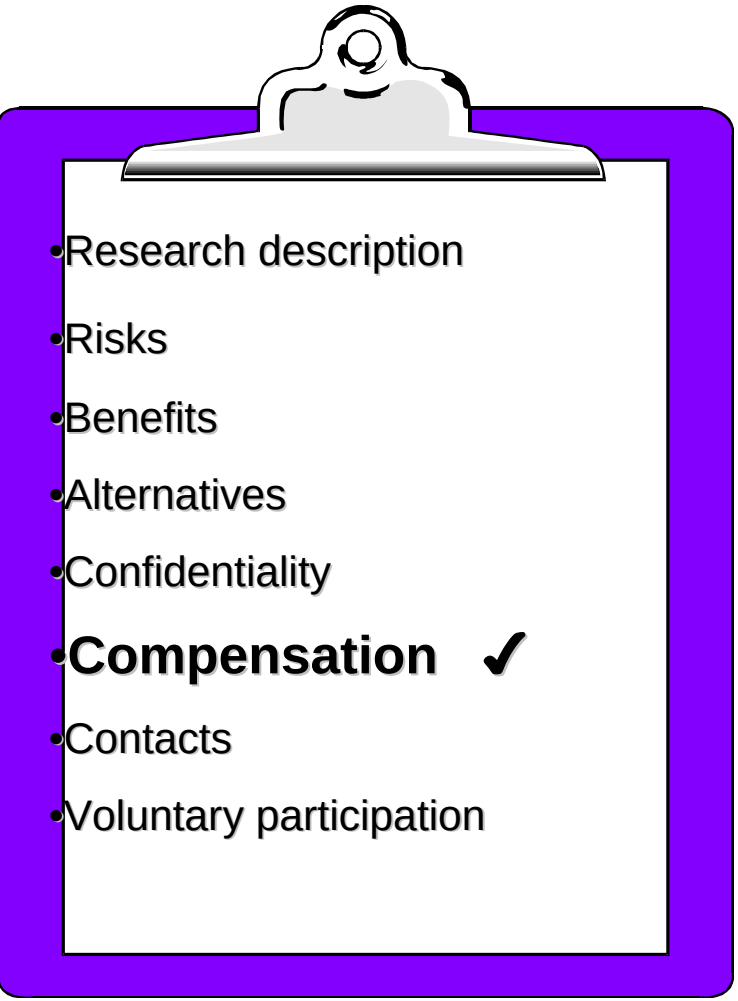
Ethical Issues in Research



- Degree of confidentiality
- Persons, organizations who may have access to the information
- How confidentiality will be maintained
- Can confidentiality be maintained (legal situation regarding mandatory disclosure to authorities)
- Where and how information will be stored and for how long

Ethical Issues in Research



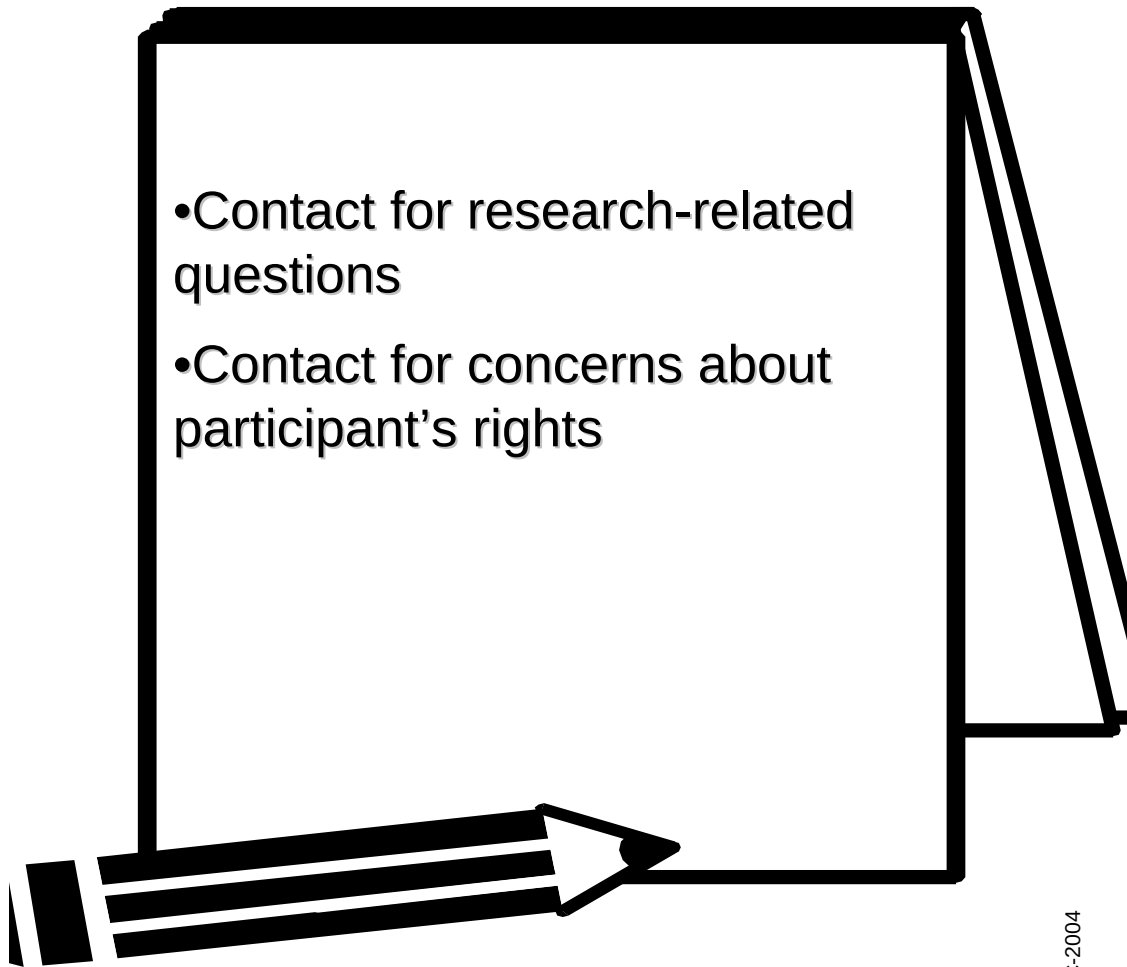
- Research description
- Risks
- Benefits
- Alternatives
- Confidentiality
- **Compensation** ✓
- Contacts
- Voluntary participation

- Available money or other forms of material goods in return for participation
- Available compensation in case of injury
- Travel cost or other expenses

Ethical Issues in Research in Reproductive Health

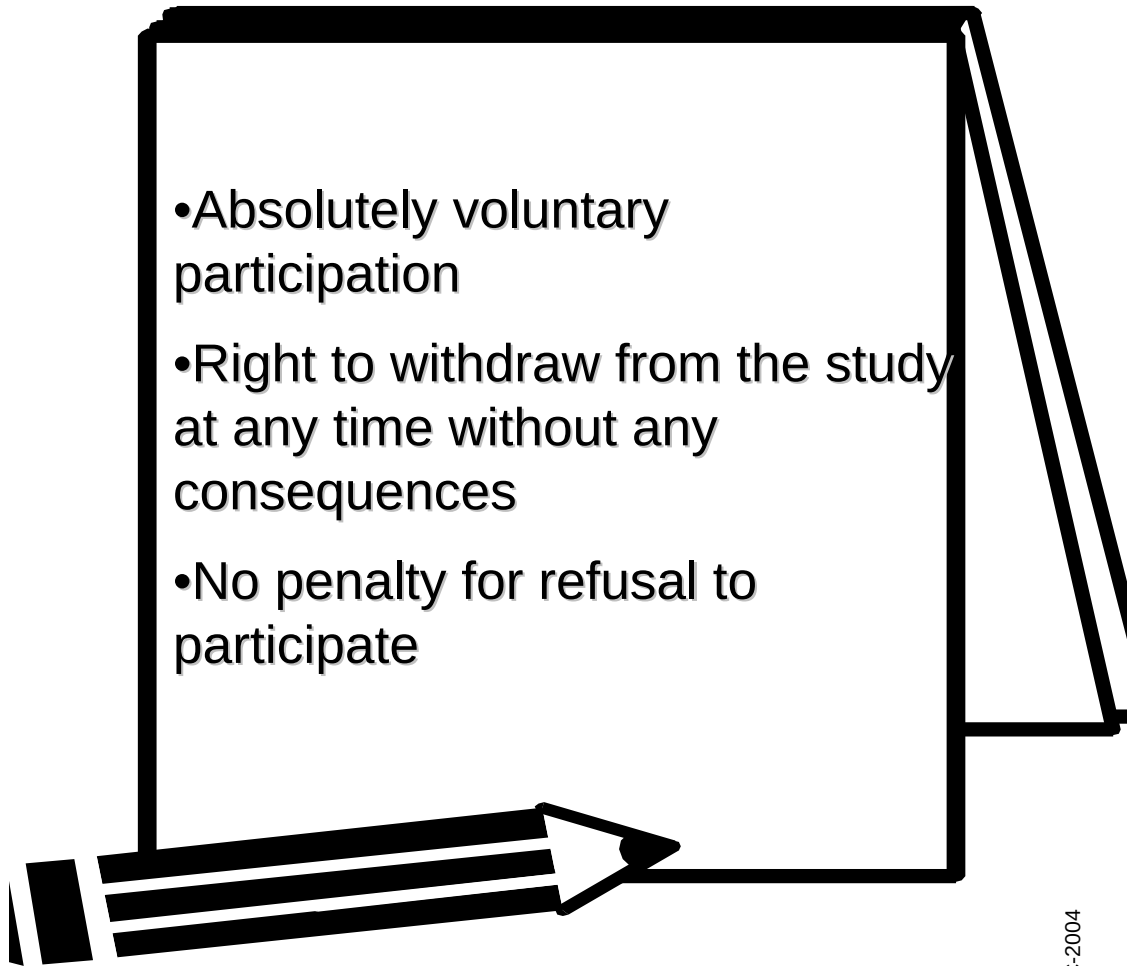
- Research description
- Risks
- Benefits
- Alternatives
- Confidentiality
- Compensation
- **Contacts ✓**
- Voluntary participation

- Contact for research-related questions
- Contact for concerns about participant's rights



Ethical Issues in Research

- Research description
- Risks
- Benefits
- Alternatives
- Confidentiality
- Compensation
- Contacts
- **Voluntary participation** ✓



- Absolutely voluntary participation
- Right to withdraw from the study at any time without any consequences
- No penalty for refusal to participate

Points to remember:

- ***avoid*** **subtly coercive statements**

  e.g. "We trust that you will agree to participate and remain in this study in order to help us find a cure for your disease"

- ***do not*** **include a line for the spouse´s signature, except under certain specific and clearly defined circumstances**

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Ethical Issues in Research

Who obtains consent

Investigator / physician

Third party (healthcare worker, interpreter)

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How to obtain cosent

- refrain from unjustified deception, undue influence

"How useful is the issue of informed consent in the Philippines and other developing countries, since it is always the poor in trials who cannot afford the drugs on the market? It is their only realistic form of treatment and they are not truly free to decide not to participate."

Quoted in Nuffield Council of Bioethics Report, 2002, p. 79

How to obtain cosent

- refrain from unjustified deception, undue influence
- seek consent after comprehension
- in general obtain signed consent (how to record)
- renew the consent of each subject if changes in conditions or procedures
- renew the consent in long term-studies at pre-determined intervals

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How to record consent

signed form as evidence -investigators to justify any exceptions to this general rule and obtain approval from the ethical review committee.

- **minimal risk**
- **subjects unwilling to sign because of fear, mistrust or suspicion**
- **signed consent forms may identify subjects in sensitive research (HIV/AIDS, CSWs, etc.)**

verbal consent/ witnessing consent

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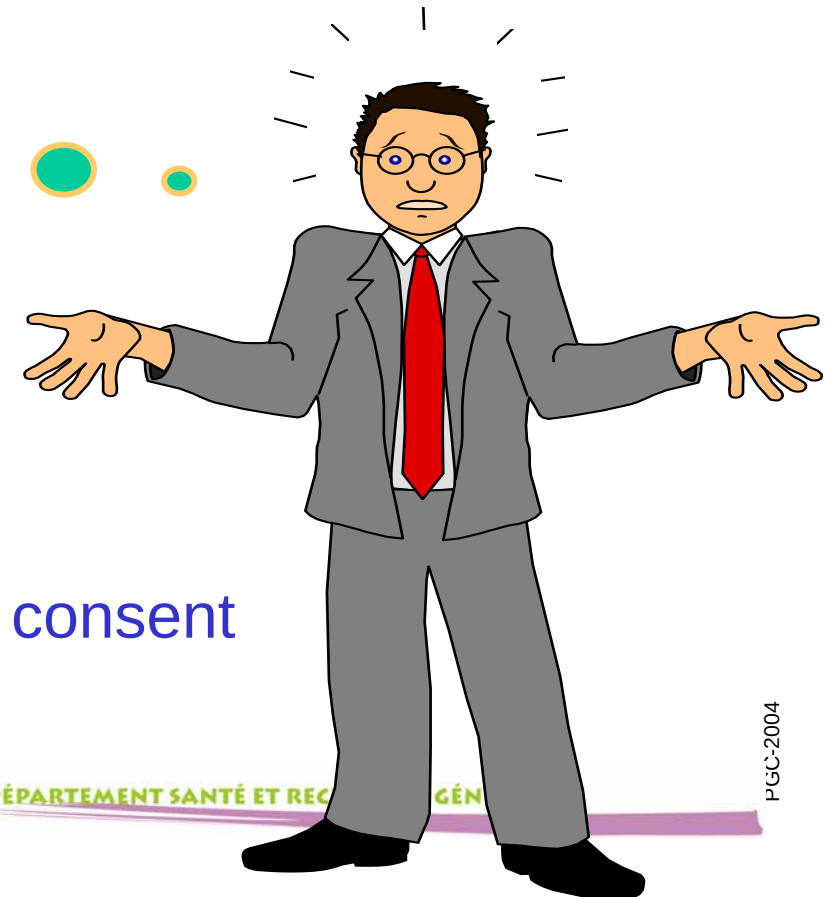
Other issues/concerns

- respect of autonomy ⟹ informed decision making
- individual versus community
  - » **community leader**
  - » **council of elders**
  - » **another designated authority**

In no case, may the permission of a community leader or other authority substitute for individual informed consent (CIOMS)

•autonomy and locus of decision-making authority

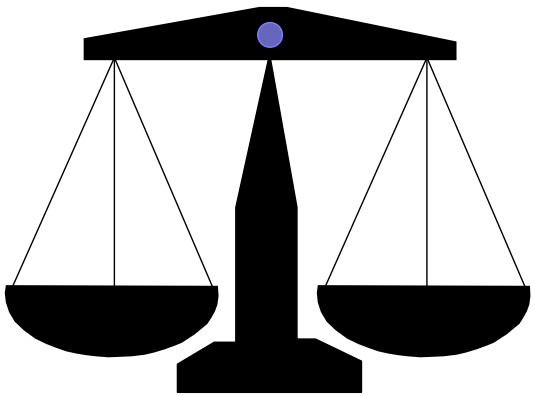
Who is making the decision?



•notion of personhood
•person versus community
•individual consent versus community consent
•women

Ethical Issues in Research

Sensitivity to cultural requirements, customs traditions



Requirement for respect for persons

...in some cultural contexts it may be appropriate to obtain agreement from the community or assent from from a senior family member before a prospective participant is approached. If a prospective participant does not wish to take part in research this must be respected. Researchers must not enrol such individuals and have a duty to facilitate their non-participation.

Nuffield Council of Bioethics Report, 2002

Other issues/concerns

- respect of autonomy ⟹ informed decision making
- impaired capacity to give adequately informed consent
  - low risk standard
  - responsible family member or legally authorised representative (case of mental or behavioural disorder)
  - ethical review committee to approve

Ethical Issues in Research

Remember - the primary ethical objective is:

- **to protect the research subject from harm**
  - **physical**
  - **psychological**
  - **social (stigmatization, community exclusion)**
  - **legal (fines)**
- **not to protect the investigator from claims**

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Ethical Issues in Research

- In research on man, the interest of science and society should never take precedence over considerations related to the wellbeing of the subject.

  » Declaration of Helsinki