GUIDANCE FOR APPLICANTS

INFORMED CONSENT

For the purposes of the Ethics Review process, the definition of Informed Consent given in the *Directive 2001/20/EC relating to the implementation of good clinical practice in the conduct of clinical trials on medicinal products for human use* is adopted. The principle of "informed and free decision" remains valid for any other kind of research.

"Informed Consent is the decision, which must be written, dated and signed, to take part in a clinical trial, taken freely after being duly informed of its nature, significance, implications and risks and appropriately documented, by any person capable of giving consent or, where the person is not capable of giving consent, by his or her legal representative; if the person concerned is unable to write, oral consent in the presence of at least one witness may be given in exceptional cases, as provided for in national legislation."

The Informed consent form must contain adequate information to meet the necessary requirements. In most cases, an information sheet should be attached. It is recommended that drafts of the consent form and the information sheet are submitted to the Commission with the application. In almost all cases the above drafts have to be available when applying for local ethics committee opinion and approval from national competent authorities, prior to the start of the proposed research.

In which cases do researchers need to make use and provide an informed consent form?

An informed consent form is required in the following cases:

When the research involves:
Patients
Children
Incompetent/Incapacitated persons
Healthy volunteers
Immigrants
Others (i.e.prisoners)
When the research uses/collects:
Human Genetic Material
Biological samples
Personal data

What type of information should be provided to the research subject:

General information:

A statement that the study involves research subjects and an **explanation of the purposes** of the research.
The **expected duration** of the subject's participation.
A **description of the procedures** to be followed/ of the **medicine** that is going to be tested, and an identification of any procedures which are experimental.
A statement that participation is **voluntary**.
Information about who is organising and funding the research.
A description of any reasonably **foreseeable risk, discomfort or disadvantages**.
A description of any **benefits to the subject or to others** which may reasonably be expected from the research avoiding inappropriate expectations.
A disclosure of appropriate **alternative procedures for treatment/diagnosis** if any, that might be advantageous to the subject.

A statement describing the procedures adopted for ensuring **data protection/confidentiality/privacy** including duration of storage of personal data.
A description of how **incidental findings are handled**.
A description of any planned **genetic tests**.
For research involving more than minimal risk, an explanation as to whether there are any **treatments or compensation if injury occurs** and, if so, what they consist of, or where further information may be obtained. Insurance coverage should be mentioned.
A reference to **whom to contact for answers** to pertinent questions about the research and research subjects' rights, and whom to contact in the event of a research-related injury to the subject.
A statement offering the subject the **opportunity to ask questions and to withdraw at any time** from the research without consequences.
An explanation of what will happen with the **data or samples at the end of the research** period and if the data/ samples are retained or sent/sold to a third party for further research.
Information about what will happen to the **results** of the research.

SPECIFIC INFORMATION:

1. Projects involving children:

Informed consent of parents/legal representative* must be obtained, but also, when the child is able to give assent, the investigator must also obtain that assent.
*The definition of legal representative should be in accordance with the legislation of the host country.

In long-term studies, where the child reaches the age of majority, the research team should obtain his/her consent to continue the study and/or for the use of samples already obtained.

A child's refusal to participate or continue participating in the research should always be respected.

Researchers should avoid exerting any pressure against the child/his-her parents that will lead to the participation of the child to the research.

Informed Consent and Information sheets are comprehensive and **separate for parents/legal representative and for children.**	
Information sheets must be in accordance to **the age of children**:	
• Information for children five years and under should be predominantly pictorial.	
• For pre-adolescent (aged up to 16) information sheets should explain briefly and in simple terms the background and aim of the study, so the child can consider assent. It also should contain an explanation that their parents will be asked for consent.	
• If an adolescent aged 16 to 18 is no longer a minor as defined in national law, or is an "emancipated minor", then written informed consent is required from these individuals.	
Assent of the child who is able to give must be required.	
Information sheets should **indicate how the study will affect the child** at home, school or other activities.	

2. Projects involving imaging procedures:

The level of invasiveness of the different diagnosis/treatment imaging procedures depends on the type of equipment, intensity of dose, repetition of exposures, subject conditions, etc. Informed consent should thus contain also information about:

Type of exposure (intensity, duration, eventual repetition) and on the eventual long-term effects.	
Use of **contrast fluid** and the eventual toxicity.	
The information sheet must include questions about patient/volunteer's **medical information**: previous treatments, presence of implants, asthma, allergy, renal failure, hypertension, claustrophobia.	

3. Projects involving incapacitated adults not able to give informed consent:

In principle, only persons able to freely understand and question, should consent. Vulnerable persons like mentally-deficient persons, severely-injured patients, etc should be excluded. However, in order to safeguard the participation of these specific groups, a special legal framework has been established. The Principle **"the interests of the patient always prevail over those of science and society,"** must be followed at all times.

In the case of clinical trials, conditions listed in the Article 5 of the *Directive 2001/20/EC relating to the implementation of good clinical practice in the conduct of*

clinical trials on medicinal products for human use, and the principles of the *Oviedo Convention* must be followed.

The informed consent must be obtained from the legal representative* if:

Consent represents the **subject's presumed will**.	
The person not able to give informed legal consent has received **information according to his/her capacit**y of understanding.	
The research is **essential** to validate data obtained in clinical trials on persons able to give informed consent or by other research methods.	
The research **relates directly to a life-threatening or debilitating clinical condition** from which the incapacitated adult concerned suffers.	
There are grounds for expecting that administering the medicinal product to be tested will produce **a benefit to the patient** outweighing the risks or produce no risk at all.	

*The definition of legal representative should be in accordance with the legislation of the host country.

In addition, all relevant requirements listed for persons capable of giving such consent shall apply.

4. Projects involving illiterate populations

When clinical trials are conducted in developing countries or communities with poor resources in developed countries, additional measures may often be needed to ensure that the objectives of informed consent are met. These measures are related to the researcher's knowledge of the local ethos. For example, in certain cases it may be appropriate to seek the agreement of a person(s) invested with a certain authority within the community.

However, **free and informed consent always has to be given by each individual involved in a trial/research**.

Where formal written informed consent from the participant is not possible, the following strategies should be used:

- Presence of a community representative trained by the scientific team.
- Witnessing the oral approval by a trained and independent community representative. He/She will verify that the purpose of the research has been explained to the participant and he/she has understood what is proposed.

WHO SHOULD GIVE THE INFORMATION? / HOW TO INFORM?

The information must be given by a physician or by other individuals with appropriate scientific training and qualifications. This point is also remarked in the Declaration of Helsinki (paragraph 14): *"After ensuring that the potential subject has understood the information, the physician or another appropriately qualified individual must then seek the potential subject's freely-given informed consent."*

Information must be given in lay terms and under no circumstances pressure of any kind should be exercised on the individual participant nor her/his family/legal custodian. The communication/information dissemination means used should be adjusted to the particularities of situation/research subject at hand.

Consent should be a **continuing process**, especially in long-term trials or projects, researchers should foster a continuous dialogue with participants and inform them of anything new related to the trial.

SOME USEFUL REFERENCES

1. Directive 2001/20/EC of the European Parliament and of the Council of 4 April 2001 on the approximation of the laws, regulations and administrative provisions of the Member States relating to the implementation of good clinical practice in the conduct of clinical trials on medicinal products for human use. OJ L 121, 1.5.2001.

2. Directive 95/46/EC of the European Parliament and of the Council of 24 October 1995 on the protection of individuals with regard to the processing of personal data and on the free movement of such data OJ 23 November 1995 No L. 281 pp. 0031-0050.

3. Council of Europe – ETS n° 164 - Convention for the Protection of Human Rights and Dignity of the Human Being with regard to the Application of Biology and Medicine: Convention on Human Rights and Biomedicine, Oviedo, 4.IV.1997. Available from: http://conventions.coe.int/treaty/EN/Treaties/Html/164.htm

4. Council of Europe – ETS n° 195 - Additional Protocol to the Convention for the Protection of Human Rights and Dignity of the Human Being with regard to the Application of Biology and Medicine, on the Prohibition of Cloning Human Beings, Paris, 12.I.1998. Available from: http://conventions.coe.int/Treaty/EN/Treaties/Html/168.htm

5. World Medical Association Declaration of Helsinki. Ethical Principles for Medical Research Involving Human Subjects. Available from: http://www.wma.net

6. Ethical considerations for Clinical Trials on Medical Products conducted with the Paediatric Population. Recommendations of the ad hoc group for the development of implementing guidelines for Directive 2001/20/EC relating to good clinical practice in the conduct of clinical trials on medicinal products for human use. 2008. Available from: http://ec.europa.eu/enterprise/pharmaceuticals/eudralex/vol-10/ethical_considerations.pdf

7. Ethical aspects of Clinical Research in Developing Countries. Opinion of the European Group on Ethics in Science and New Technologies to the European Commission, 2003.

8. International Ethical Guidelines for Biomedical Research Involving Human Subjects. Council for International Organizations of Medical Sciences (CIOMS) ISBN 92 9036 075 5. Available from: http://www.cioms.ch/frame_guidelines_nov_2002.htm

9. Information Sheets & Consent Forms. Guidance for Researchers and Reviewers. Version 3.2 May 2007. National Patient Safety Agency. National Research Ethics Service. Available from: http://www.nres.npsa.nhs.uk/rec-community/guidance/#InformedConsent

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11. Consent: patients and doctors making decisions together, June 2008. General Medical Council. Available from: http://www.gmc-uk.org

12. H El-Wakeel, G J Taylor, J J T Tate. What do patients really want to know in an informed consent procedure? A questionnaire-based survey of patients in the Bath area, UK. J Med Ethics 2006; 32:612–616.

13. Delany C. Making a difference: incorporating theories of autonomy into models of informed consent. Journal of Medical Ethics 2008;34:e3; doi:10.1136/jme.2007.023804