The European Commission's 7th Framework Programme (2007-2013) is now in force. A hugely increased budget is available for research projects but with this comes added responsibility. **Mary Fitzgerald** of the Commission's ethics review team explains the ethical requirements in FP7, what these mean for applicants looking for funding and the importance of getting it right first time!

The EU gets tough on ethics

MAIN POINTS

- An ethics review will be carried out on proposals submitted to FP7
- Proposals that ignore ethical concerns will be rejected
- Submit drafts of information sheets and consent forms with your proposal
- Identity and contact the ethics expert in your organisation now

Ethics is central to scientific integrity. This truism is set in stone in the European Commission's 7th Framework Programme for Research (FP7) which has just come into force. A key pillar of FP7 is ethics review: research proposals that have successfully come through the scientific evaluation are subject to an ethical evaluation. Through this, the public's concerns relating to science are represented and addressed.

What this means for all consortia submitting proposals under FP7 is that ethical concerns must be identified and addressed within the proposal. This is the responsibility of you, the applicant. Proposals that ignore ethical concerns will be rejected – the Commission will not get back demanding information. If proposals make a credible attempt to address ethical issues but don't cover all issues, then clarification may be sought and a re-submission granted. But re-submissions invariably mean delay in time to contract. The message is: Get it right first time.

What follows is not an academic textbook on ethics, but a pragmatic guide to help researchers grasp the basics and apply them with confidence.

THE ETHICS REVIEW TEAM

I am a member of the Commission's ethics review team, which is part of the Governance and Ethics unit. Peteris Zilgalvis, a Latvian lawyer and expert in bioethics, is head of unit. Also on the team are a French research immunologist and a Belgian graduate in bioethics. I myself am a UCC science graduate and Open University law graduate. So our team is diverse in nationalities and skills.

The first thing to note is that the ethics review team does not actually undertake the ethical review! Our role is to organise the ethics review process. We represent the Commission and our task is to ensure that the review is undertaken in compliance with FP7 rules.

We rely on the skills of external reviewers to read proposals for ethics review and identify potential problems. Reviewers are chosen from database of experts that is open to anyone with an interest in reviewing science or ethics. To be a reviewer you must register (on https://cordis.europa.eu/emmfp7/index.cfm?fusection=wel.welcome). There are about 50,000 experts registered with a diverse range of skills; lawyers, clinicians, IT specialists, philosophers, theologians. All panels need to be representative of the European Union countries, have a reasonable gender balance, and introduce new blood.

What are ethics reviewers looking for in proposals? What risks and shortfalls do you, the applicant, need to avoid? This article addresses these questions.

UNDERSTANDING 'ETHICS'

Ethics is often misunderstood in the realm of research. It is closely linked with law, rules and regulations but it is not adversarial: 'Ethics v Research'. Ethics reviews at the Commission aim to be collaborative and constructive. Considering ethical issues from the concept stage of a proposal enhances the quality of research.

Ethics is context-dependent, consequently definitive mathematical outcomes are rare. Your proposal must clarify the necessity to use personal data, animals, human tissue and the involvement of human beings. Do not assume that the reputation of your institution or of your publications is sufficient to exempt your proposal from describing these elements. In one case in my experience a researcher submitted a proposal to study bone regeneration after a fracture – this involved breaking animal bones. Under questioning it emerged that the researcher had given no thought to the ethical implications but simply counted on the reputation of the institution. Don't assume! Address issues at submission stage.

Take time to consider the benefit/burden balance of each work package. Consider the impact of the research, not only in terms of scientific advancement (publications, patents etc) but also in terms of human dignity and social and cultural impact.

‘Ethics is state of mind. Ethical sensitivity is directly related to honesty and truthfulness.’

Ethical sensitivity is a measure of the honesty and clarity of the proposal - and is the unwritten skill that ethics panels search for. What is sought is a full consideration of the issues and a serious attempt to minimise harm. Casual, shoddy dealing is immediately recognisable as such. 'Copy and paste' ethics does not work.

ETHICS - IT'S A STATE OF MIND

Ethical sensitivity is directly related to honesty and truthfulness. Applicants should ask themselves: How would I like my spouse/child/parent's dignity to be handled in a research setting? Do consider the social impact of the research. (See panels: **Informed consent** and **Data protection and privacy**) For instance, will the outcome have a dual use (see panel **Dual use**) that could pose a threat to personal security, privacy and human dignity?

The use of animals in research is still necessary. The approach to animal research must be rooted in the application of the 3 Rs (Replace, Reduce and Refine). If a procedure would hurt the researcher, you should assume that it would also hurt the animal (see **Animal welfare**).

FP7 provides vast opportunities to include developing countries. EU ethical regulations should be equally applied and upheld in these countries. Such standards may not yet be the norm in certain countries - the aim is to see vast improvements by the end of FP7 (in 2013). An important objective of the Governance and Ethics unit is facilitating capacity-building in developing countries (see **Research in developing countries**).

WHICH PROPOSALS ARE REVIEWED?

Ethics review is undertaken on selected proposals that have successfully come through the scientific evaluation. Scientific evaluators identify the proposals needing ethical reviews.

Ethics review is automatic for proposals which include a research intervention on human beings, and/or the use of human embryonic stem cells (hESC) and/or use of non-human primates.

What is the objective? The ethics review aims to prevent Community funding being used for research activities that contravene fundamental rights.

Are the results reported? Yes, every proposal undergoing ethics review is provided with a report outlining the views of the panel. There is no numerical marking system similar to the scientific evaluation. If it is considered that the proposal has not clarified all the ethical issues properly clarification may be sought and a resubmission may be granted.

Resubmissions will only be granted to proposals that have made a significant attempt to address ethical issues. Resubmission invariably means delay in time to contract.

INFORMED CONSENT

Research involving human subjects is important for science. The Nuremberg code first enunciated the concept of voluntary participation and has become a central dogma in key international declarations. Informed consent is not confined to medical research, it applies to all human participation in research.

Each participant in a research project, prior to consent, should be clearly informed of its goals, its possible adverse events and the possibility to refuse to enter or to retract without adverse consequences. In addition, no inducement should justify the participation in research.

Who should consent?

Only persons able to freely understand and question.

Vulnerable persons (prisoners, mentally ill, children) are excluded, although their participation in studes can be accommodated if they benefit directly. In such cases, obtaining informed consent requires special attention and involves the next of kin or legal and medical representatives.

How to inform?

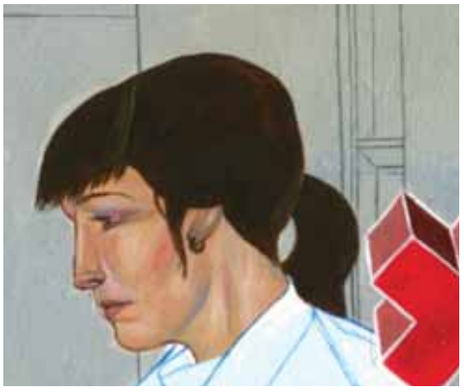
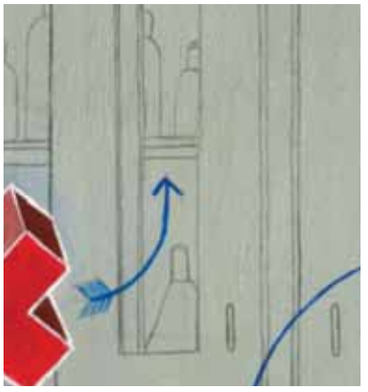
This is a challenging task, requiring sensitivity and attention. The type of language used must be clear and uncomplicated. In general you should pitch at the understanding of a 12 year old, and consider using linguists or psychologists. Researchers should explain what happens to data, samples, or recordings once the research project is completed. Ensure that if data/samples are intended for further use in other research projects that this is stated in the consent form.

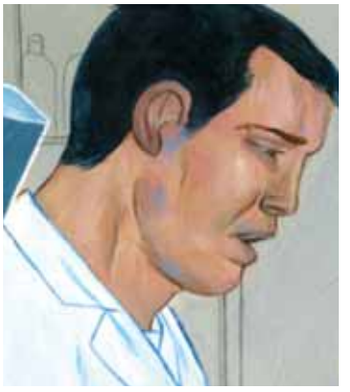
How to get approval?

This is directly related to a person's vulnerability, independence, intelligence, culture and traditions. The presence of some form of witness is advised – perhaps a community representative, family member, or legal representative in the case of a mentally ill.

The informed-consent form should address the following issues:

– The purpose of the research, the duration, procedures to be used, and identification of



any procedures which are experimental;
– A description of the foreseeable risks or discomforts that are reasonably expected;
– A description of any benefits to the subject or to others which are reasonably expected;
– A disclosure of any appropriate procedures that might be advantageous;
– A statement describing the extent to which confidentiality of records identifying the subject will be maintained
– 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 can be obtained;
– Identify the contact person for answers to questions about the research and research subject's rights, and whom to contact in the event of injury to the subject; and
– A statement that participation is voluntary, withdrawal from the research can be undertaken at any time without loss of benefits which the subject is otherwise entitled to.

NOTE: The above applies to the use of human tissues too.

DATA PROTECTION AND PRIVACY

Privacy problems exist wherever uniquely identifiable data relating to a person is collected or stored, in digital form or otherwise. Improper disclosure control can be the root cause for privacy issues. The most common sources of data that are affected by data privacy issues are:
– Health Information
– Criminal Justice
– Financial Information
– Genetic Information, and
– Location Information.

The challenge in data protection is to share data while protecting the personally identifiable information. This is done by using aggregate data, or coding, or making data anonymous.

The Directive on the protection of personal data contains a number of key principles which must be complied with. Data must be:
– Fairly and lawfully processed
– Processed for limited purposes
– Adequate, relevant and not excessive
– Accurate
– Not kept longer than is needed
– Processed in accordance with the data subject's rights
– Secure, and
– Not transferred to countries without adequate protection.

The definition of processing incorporates the acts of 'obtaining', 'holding' and 'disclosing'.

Key ethical issues that need to be addressed in proposals are the informed consent for processing the data, and the arrangements for protecting the confidentiality of personal data of the individual concerned. If data is retained for further research the consent form should be consistent with this fact. Applicants dealing with banked biomaterial should also reflect on the privacy and consent issues.

ANIMAL RESEARCH

At the time of writing the Directive 86/609/EEC is being reviewed. Researchers using animals are encouraged to contribute to this current debate. Contact your National Contact Point.

Animal research is primarily associated with medical research. It is a topic of high sensitivity and each proposal must convincingly show that it has reflected on and properly applied the 3 R principles:

Reduction refers to methods that enable researchers to obtain comparable levels of information from fewer animals, or to obtain more information from the same number of animals.

Replacement refers to the preferred use of non-animal methods over animal methods whenever it is possible to achieve the same scientific aim.

Refinement refers to methods that alleviate or minimise potential pain, suffering or distress and enhance animal welfare.

Whilst paradoxical, it is possible that the use of x number of animals may be permitted in one experiment/proposal and considered excessive in another. This is due to the context of the experiments; it may occasionally be unethical to use fewer animals if the results produced are insignificant.

Details of the species, strain and origin should be provided and a brief explanation of why they have been chosen. Provide a clear explanation of the anticipated benefits of using animals and why alternative methods cannot be used. State the number of animals involved. Consider the benefit/burden of the experiment and address issues of pain and suffering. Address what happens to the animals at the end of the experiment - are they used again or humanely killed?

If a transgenic animal is being created further ethical issues arise, such as second

generation follow-up, and the capacity to deal with animals born with health problems.

RESEARCH IN DEVELOPING COUNTRIES

Research undertaken in developing countries should comply with the highest ethical standards. Current reality does not always permit this in practice due to cultural, social and economic reasons. However, capacity-building for ethics compliance is a key objective for the Governance and Ethics unit. During the implementation period of FP7, significant improvements will be demanded and supported.

You must justify the involvement of developing country.

When involving a developing country the following items must be considered:

– Culture & literacy
– Best interest of the subject
– Informed consent – if written consent forms are difficult because of illiteracy etc, consider some form of recording. One of the most innovative approaches I've come across was a video of the village chief informing his community about a research project.
– Benefit sharing
– Use of local resources – plants, human samples, data, animals
– Avoiding double standards.

RESEARCH ON HUMAN EMBRYONIC STEM CELLS (HESC)

Research on hESC constitutes a very small percentage of the proposals funded. However, although few in number, the ethics review is particularly rigorous. Ensure that hESC research is permitted in the Member State/Country concerned. The Scientific Evaluation determines the necessity to use hESC. Assuming necessity is established the proposal proceeds to ethical review which will assess the following:

– The proposal does not include research activities which destroy embryos, including for the procurement of stem cells.
– Whether the consortium has taken into account the legislation, regulations, ethical rules and/or codes of conduct in place in the country(ies) where the research using hESC is to take place, including the procedures for obtaining informed consent.
– The source of the hESC
– The measures taken to protect personal data, including genetic data and privacy
– The nature of financial inducements, if any.

DUAL USE

Dual use is a term often used in politics and diplomacy to refer to technology which can be used for both peaceful and military or terrorism aims.

The most serious ethical concerns are linked to those technologies which potentially result in an invasion of privacy through surveillance activities. Such a scenario could constitute an infringement of fundamental human rights and raises ethical concerns that must be addressed.

Ethical sensitivity is shown by questioning if human life is endangered by the research outcome. Reasonableness and proportionality are central to determining if research raises a genuine dual use concern – i.e. every chemical/microbiology laboratory has sufficient armoury to destroy a population yet it is understood that such situations are not interpreted as dual use risks.

CONCLUSION

The launch of FP7 has given rise to a flurry of activity within the research community. Researchers are scanning deadlines, seeking collaborators, scrutinising financial rules. But don't forget research ethics.

When considering ethics, you need to be practical, profound, contextual, and creative. Researchers often discuss the ethical criteria of FP7 as if they were financial guidelines; they want to be given specific directions along the lines of: 'The Commission allows a maximum of x mice in any one work package'. Ethics doesn't work like this, everything depends on context.

Similarly, I always wonder why consortia submit legislation to support their ethics. What is this legislation meant to do? Convince the panel that since you can produce the law, you can apply it? I'm reminded of the red traffic light: I know I must stop at the light but I can't tell you what piece of legislation states this, and having a copy of the Road traffic act would not increase anybody's confidence in my driving!

The Commission cannot provide direct instructions on how to handle all aspects of ethics. It is for the researchers to illustrate their integrity and convince the panel. Honesty is the best policy. TI

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COMMON PROBLEMS

Certain common errors appear frequently in proposals. Do take time to address these issues in your information sheets and consent forms - they are not particularly difficult to avoid.

The Commission is concerned about the risks and liability associated with research, particularly clinical trials. Mention the broad details of your insurance coverage.

'Incidental findings' refer to the medical problems discovered in the course of a research/clinical trial which were not related to the topic of research. It is necessary to declare how you will deal with such findings. There is no right or wrong answer; different research groups have different approaches. It is imperative that the research subject is made aware of the approach being taken.

Avoid situations that could be construed as giving rise to a conflict of interest – for instance, a treating physician who is involved in a research activity should not be the person to inform the subject about the pros and cons of the clinical trial.

You must fully disclose incentives. Financial incentives are the most common but others exist; in a developing country money may not be the most common incentive. No definitive answers exist - the right approach depends on the context.

You must also confirm to the subjects that leaving the study will not have adverse consequences.

The involvement of children is very sensitive. Identify if there is a direct benefit to the individual child. If this individual benefit is not present and children need to be involved in a study, it is necessary to ensure that the procedure carries a minimum risk for the child and a minimum burden is placed on a child.

Numbers, species and origin of animals need to be specified. Identify what happens at the end of the research project. It could be embarrassing to assert that no alternatives were available to your animal work without checking relevant databases.