

# Ethical Evaluation of Research Proposals by Ethics Panels Advising the European Commission

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**Summary** — Ethical principles with regard to animal experimentation are referred to in European Union (EU) legislation and other official documents. Therefore, applications for funding of research under the EU's research programme may undergo an ethical review that is carried out by so-called ethics panels, consisting of experts chosen by the European Commission. The work of these panels differs substantially from that of other ethical committees, as they exist on the institutional, local, regional or national level. Their main purpose is not to decide whether a proposed research can be regarded legal, and therefore should be endorsed or licensed; instead, it is to help the Commission in prioritising its funding. The panels may examine other ethical aspects than those of animal experimentation or animal welfare alone, such as the use of human volunteers. This is reflected by the composition of the panels. Their decisions are normally based on consensus. Even though these decisions may refer to EU legislation, the criteria applied are not restricted to those provided by this legislation. Nevertheless, the various aspects of the Commission's ethical evaluation system (e.g. formal and practical basic conditions, information content of applications, type of decisions taken, lacking of any quality control) offers opportunities for improvement.

**Key words:** *animal experiment, ethical committees, ethics, Fifth Research Framework Programme of the European Commission, legislation.*

## Introduction

Ethics panels advising the European Commission do not represent the most common type of ethical committee. It is not their task to decide on the legitimacy of a proposed research. Instead, they are aimed at evaluating, from an ethical point of view, applications for funding of research, and thus help the Commission in deciding whether a specific research proposal deserves to receive financial support.

These panels were set up in 1997, for the first time by the Commission, in response to growing public concern and pressure from the European Parliament concerning the need to guarantee the ethical acceptability of Commission-funded research. The present paper is partly based on the personal experience of an animal protection representative on those panels, but one focus of the following analysis is in legislation and other objective factors that determine the composition, functioning and impact of the panels. It should also be noted that reference is only made to animal welfare aspects, whereas these represent just one out of many ethical issues in research, relevant legislation and the scope of work of the panels.<sup>1</sup>

## Formal Framework

The formal framework in which the ethics panels operate is given by the legislation covering the aspects the panels are to evaluate on the one hand, and the specific demands given within the Fifth Research Framework Programme of the European Union (EU), on the other hand.

## Relevant legislation

### *The Treaty of Amsterdam*

An EU Heads of Member State meeting in Amsterdam in 1997 agreed to include a special legally binding protocol on animal welfare in the new EU Treaty (the so-called Amsterdam Treaty). This protocol introduced a clear legal obligation for all Community institutions to pay full regard to the welfare of animals (2).<sup>2</sup>

This animal welfare protocol not only obliges the Commission and the Member States of the EU to pay attention that existing EU legislation is properly enforced, it also asks for appropriate consider-

<sup>1</sup>Out of 143 research proposals under the EU's Fifth Research Programme from 1999 to 2001 that were submitted to an ethical review, 29 involving non-human primates and 14 involving other animals were examined by the ethics panels (1).

<sup>2</sup>"In formulating and implementing the Community's agriculture, transport, internal market and research policies, the Community and the Member States shall pay full regard to the welfare requirements of animals, while respecting the legislative or administrative provisions and customs of the Member States relating in particular to religious rites, cultural traditions and regional heritage".

ation of animal welfare principles in all aspects of the functioning of the EU and in drafting future (from 1998 on) legislation or decision-making.

#### *Council Directive 86/609/EEC*

The most relevant piece of legislation to look at in the present context is obviously *Council Directive 86/609/EEC regarding the protection of animals used for experimental and other scientific purposes* (3). This Directive lays down the basic principles to take into account by the EU Member States in drafting their national legislation on animal experiments. Its main principles are:

- experiments must be indispensable for specified purposes;<sup>3</sup>
- pain, suffering or distress must be ethically justifiable;<sup>4</sup>
- choice of species must be justified;<sup>5</sup> and
- the Three Rs must be applied.<sup>6</sup>

Remarkably, genetic engineering of animals falls under the Directive's definition of an animal experiment.<sup>7</sup>

#### *Council Decision of 23 March 1998*

In addition to these requirements the need to reduce animal experiments on non-human primates is mentioned in *Council Decision of 23 March 1998 concerning the conclusion by the Community of the European Convention for the protection of vertebrate animals used for experimental and other scientific purposes* (4).<sup>8</sup>

### **The Fifth Research Framework Programme**

Funding of research within the EU, i.e. via the Commission, is based on the so-called Research Framework Programmes (RFPs). The current Fifth RFP started in 1998 and ends in 2002.<sup>9</sup> The EC has a budget of about 15 billion Euros to spend in the Fifth RFP (5).

Not only researchers from EU Member States are eligible to apply for funding under the Fifth RFP. It is also open to researchers from third countries, in particular the accession countries that will become members of the EU in the coming years. One must bear in mind that these countries may not yet have legislation in place that would conform to the actual EU legislation currently in force.

Some of the following information refers to specific programmes within the Fifth RFP, in particular the *Quality of Life and Management of Living Resources Programme*, under which a major part of projects in the biomedical sector is funded.

#### *Ethical principles within the Fifth RFP*

In several documents referring to the Fifth RFP, ethical aspects are addressed. The most relevant document in this regard is probably the decision in which the Fifth RFP is constituted (6), i.e. *Decision No 182/1999/EC of the European Parliament and of the Council of 22 December 1998 concerning the Fifth Framework Programme of the European Community for research, technological development and demonstration activities (1998 to 2002)*.

Article 7 of the Decision states that, "All research activities conducted pursuant to the fifth framework programme shall be carried out in compliance with fundamental ethical principles, including animal welfare requirements, in conformity with Community law".

<sup>3</sup>Article 7.2. *An experiment shall not be performed if another scientifically satisfactory method of obtaining the result sought, not entailing the use of an animal, is reasonably and practicably available.*

<sup>4</sup>Article 12.2. *Where it is planned to subject an animal to an experiment in which it will, or may, experience severe pain that is likely to be prolonged, that experiment must be specifically declared and justified to, or specifically authorized by, the authority. The authority shall take appropriate judicial or administrative action if it is not satisfied that the experiment is of sufficient importance for meeting the essential needs of humans or animals.*

<sup>5</sup>Article 7.3. *When an experiment has to be performed, the choice of species shall be carefully considered and, where necessary, explained to the authority.*

<sup>6</sup>Article 7.3. *In a choice between experiments, those that use the minimum number of animals, involve animals with the lowest degree of neurophysiological sensitivity, cause the least pain, suffering, distress or lasting harm and that are most likely to provide satisfactory results shall be selected.*

<sup>7</sup>Article 2(d). *"Experiment" means any use of an animal for experimental or other scientific purposes which may cause it pain, suffering, distress or lasting harm, including any course of action intended, or liable, to result in the birth of an animal in any such condition.*

<sup>8</sup>(Preamble) [3]. *The use of primates for experimental and other scientific purposes carries the risk of suffering for those animals and therefore has to be reduced.*

<sup>9</sup>In 2002, the Sixth RFP was established; it involves an evaluation process that has been changed in some respects compared to that of the Fifth RFP. The present paper is restricted to the evaluation process under the Fifth RFP.

In that decision, an important piece of information can be found within a footnote in its ANNEX II, *General outlines of community activities, scientific and technological objectives and related priorities*:

*To the extent possible, animal experiments and tests on animals should be replaced with in vitro or other alternative methods. Modification of the genetic heritage of animals and animal cloning will be envisaged within the current framework programme only for objectives that are justified on ethical grounds and to the extent that the operations involved are affected on an ethical basis, with respect for the well-being of animals and the principles of genetic diversity. (The practical effects of this will be further elaborated in the specific programmes.)*

Apart from being hidden in an Annex's footnote, the relevance of this important clause is limited, as it specifically refers to transgenesis and cloning.<sup>10</sup>

### The European Group on Ethics

The Commission has a body in place to advise it on ethical aspects of science and new technologies in connection with the preparation and implementation of Community legislation or policies, the European Group on Ethics (EGE), formerly the European Group on Ethics in Science and New Technologies. This group has issued a number of so-called "opinions" in this context. In their opinion no. 10, the group has considered "The ethical aspects of the Fifth Research Framework Programme" (7).

In this opinion, the Three Rs are named as the basic ethical principle for animal experimentation

(although the definition given for refinement is not consistent with the common definition, the need to minimise suffering is mentioned separately), and research on non-human primates (even though these are not explicitly mentioned) and transgenesis or cloning of animals are seen as issues that would require specific consideration.<sup>11</sup>

### Ethics Panels

To fulfil the demands of this formal framework, the Commission uses the so-called ethics panels (or ethical review panels). The review of research proposals by these panels is embedded in the proposal selection process that consists of a number of steps. In Figure 1, the different stages are presented in a simplified scheme.

The ethical review panels come in at a late stage of the selection process, and their task is to evaluate whether specific research proposals that have passed the evaluation by scientific panels comply with ethical principles.

There are several issues that, if they are touched by a proposal, automatically require an ethical review. An ethical review may also be undertaken as a consequence of the identification of other ethical concerns during the scientific evaluation of a proposal.<sup>12</sup> The genetic engineering and cloning of animals and the use of non-human primates are seen as specific issues that would require an ethical review, whereas animal experimentation as such is not. This is despite the fact that neither legislative nor other formal demands give any indication if and/or how to prioritise animal experimentation issues. Only the above-mentioned opinion of the EGE has highlighted these two issues.

<sup>10</sup>"[2] Taking account of the declaration of the European Council of Amsterdam and the European Parliament resolution on the banning of human cloning [OJ C115, 14.4.1997, p. 92] and of relevant Community legislation, research conducted at Community level will be carried out, taking account of the competent authorities, in particular the European Group on Ethics in Science and New Technologies and the Human Embryo and Foetus Protection Group, as well as the opinions of relevant international organisations, whilst respecting the principles laid down in the Helsinki Declaration and the relevant resolutions of the World Health Organisation (WHO) and in other relevant international Conventions. No research activity which modifies or is intended to modify the genetic heritage of human beings by alteration of germ cells or by acting at any other stage in embryonic development and which can make such alteration heritable will be carried out under the present framework programme. In the same way, no research activity, understood in the sense of the term 'cloning', will be conducted with the aim of replacing a germ or embryo cell nucleus with that of the cell of any individual, a cell from an embryo or a cell coming from a late stage of development to the human embryo".

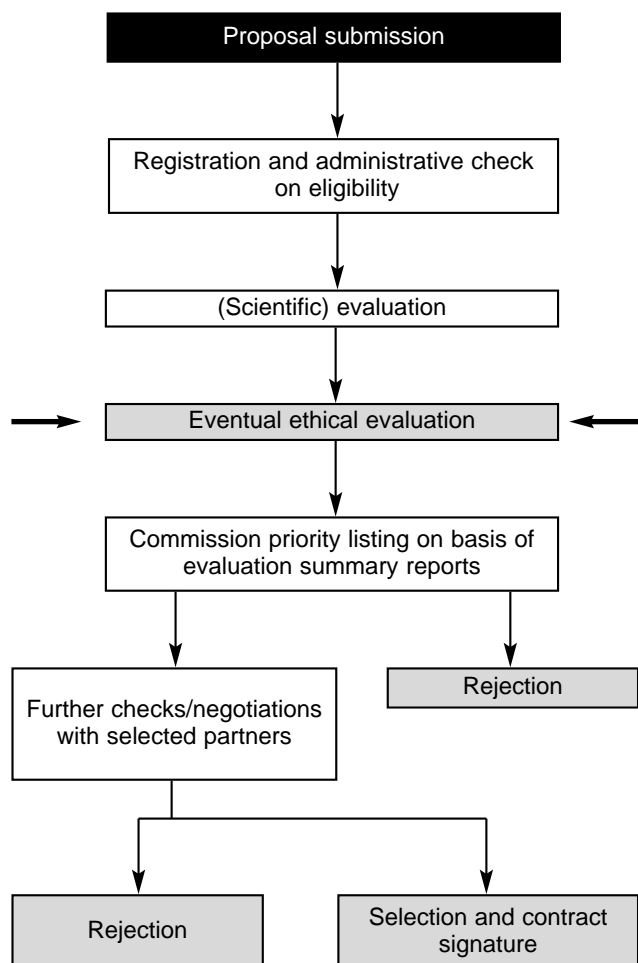
<sup>11</sup>"With regard to animal experimentation, the ethical principles applicable are in particular:

- replacement (by alternative methods);
- reduction (in the number of animals);
- refinement (making it possible to limit the number of experiments).

*Animal suffering must be avoided or kept to a minimum taking into account the benefits expected from the research. These principles must be applied particularly rigorously to the animal species that are the closest to human beings. Research involving transgenesis and/or the cloning of animals calls for a particularly high level of ethical vigilance".*

<sup>12</sup>"An ethical review has been implemented systematically for proposals proposed for funding following the scientific evaluation dealing with sensitive issues, in particular where Member States legislation differs such as regarding the use of human embryos, human fetuses, embryonic or foetal tissue and the use of non-human primates. Furthermore, any proposal for which other ethical concerns have been identified during the scientific evaluation such as genetic screening; clinical trials in developing countries; clinical trials involving healthy volunteers, children and/or persons unable to give consent are reviewed" (1).

**Figure 1: Proposal selection process in the Fifth RFP**



Adapted from reference 9.

## Experts

The expertise of the individuals that constitute an ethics panel and the ratio of the different participants is not precisely defined. There are, however, several Commission documents that give an indication in that regard. Whether ethics panels should be composed of “scientists, lawyers, philosophers, academic specialists in ethics, specialists in animal protection” (8) or represent “a variety of different disciplines (biology, genetic, neurosciences, medicine, psychology, law, philosophy, theology, sociol-

ogy, animal welfare groups)” (1), there is an obvious intention to involve experts with various backgrounds and different interests.

One may question the role of the scientists with a biomedical background. They must not necessarily be qualified in the ethical issues that are raised by a proposal. Whereas they can play an important role in resolving scientific questions that come up during a review, it is also clear that they cannot be expected to be unbiased with respect to the evaluation of animal use, particularly when they are involved in animal experimentation themselves.

Other criteria depicting the panel composition are the same as for other types of expert panels the Commission employs for the selection of research proposals. These are mainly:

- geographical backgrounds;
- linguistic capabilities;
- gender; and
- impartiality.<sup>13</sup>

The Commission recruits experts for participation in ethics (and other) panels. The Commission has published a call for applications, which remains open for the duration of the Framework Programme. Interested individuals fill in an application form describing their background and competence (consisting of a *curriculum vitae* and appropriate keywords). The Commission selects appropriate applications, and these are entered into a database. The Commission services then select experts from this database to participate in the evaluation of research proposals.

Normally, a panel consists of about 10–15 individuals who meet in Brussels for 2–4 days to evaluate about 10–20 research proposals. These meetings are confidential; and therefore, this article does not contain any specific information on individual experts nor on the particular content of research proposals.

## Applications

Researchers who plan to submit research proposals to the European Commission under the Fifth RFP are provided with guidance documents on how to apply. These documents, which are specific for the different thematic programmes, also refer to ethical aspects of the proposed research.

<sup>13</sup>“Care will be taken to ensure that each panel of experts has an appropriate range and balance of competences, geographical backgrounds and linguistic capabilities. As far as possible, attention will also be given to achieving an appropriate gender balance . . . In general, and in order to help the Commission, panels of independent, external experts will be constituted covering a wide range of relevant expertise, without linguistic or geographic bias” (9).

In the *Guide for Proposers, Part 1, Quality of Life and Management of Living Resources* (8) proposers are made aware of the need to describe the ethical implications of their research.<sup>14</sup>

As mentioned before, animal experimentation is just one issue in this context. Other issues are e.g. the use of human embryos or fetal tissues, pharmaceutical studies on volunteers, children, and so on.<sup>15</sup>

The demands on research proposals that involve animal experimentation are also specified in the *Guide for Proposers*:

- *proposers should specify and justify the type and number of animals to be used and indicate why other methods cannot be used for the research;*
- *so as to indicate what steps they have taken to comply with the principles of reduction, refinement and replacement;*
- *and describe why the potential benefits of the research should be seen to outweigh the harm to the animals used.*

If non-human primates are to be used in a proposed research highly specific information on several aspects is required.<sup>16</sup>

If animals are to be genetically modified the only specific requirement mentioned in the *Guide for Proposers* is to describe how the anticipated benefits justify any possible suffering to animals.<sup>17</sup>

This raises the question how these requirements are reflected in the actual research proposals that are to be evaluated. The following analysis is based on the personal experience of the author. The proposals serving for this analysis differed quite significantly in their response to the mentioned requirements. The pointing at the deficiencies of proposals rather than on positive aspects is not to generalise, but to refer to the difficulties in the work of the ethics panels.

The major problem with a large number of proposals is (or has been) that the following type of

information was either not given at all, or was given in an insufficient way:

- estimated pain, suffering or distress;
- justification for species chosen;
- benefit/ethical justification; and
- application of Three Rs.

A typical example of insufficient information is when in a research proposal, the use of animals has been mentioned, but the specific procedure they have to undergo remains unclear, and therefore, all other types of information that would be needed for an ethical evaluation cannot be deduced from the proposal.

Sometimes, especially in big projects, information is given on some type of animal use, but not for another. This is particularly a problem with project clusters in which a large number of institutes participate. Proposals for such clusters may lack a comprehensive outline of the animal use for the whole project. The evaluators then have to collect the information from the description of the proposed research for each individual project partner. Normally, the different project partners provide highly heterogeneous information, reflecting either their level of awareness for ethical problems or for the fact that the evaluation of this information may represent a factor in the proposal selection process. An overall evaluation of the entire project cluster is then particularly difficult to make.

## Ethics Panel Meetings

### Evaluation process

For the evaluation, the nominated experts come together in a Commission building in Brussels. The

<sup>14</sup>— “Have relevant ethical issues been adequately taken into account in the preparation of the proposal?”  
— “Is the proposed research compliant with fundamental ethical principles, if relevant?”

<sup>15</sup>Footnote 18: “. . . projects involving the use of human embryos or foetal tissues, or experimentation on non-human primates, as well as any project where the evaluators will express concern with regard to ethical aspects of the research (its objectives, methodology or potential implications)”.

<sup>16</sup>— “If the research involves non-human primates:  
— . . . specify which species are used  
— what are their origin  
— if they are caught wild  
— which partner is in charge of the importation, or breeding of animals  
— where the primates are located and  
— which partner is performing the experiments, and  
— how many animals are sacrificed”.

<sup>17</sup>— “In case of genetic modification of plants or animals:  
— Describe how the anticipated benefits justify any possible suffering to animals . . . or any possible risks to human health or the environment, and the implications for biodiversity”.

Commission formally moderates the panels, but it selects one of the attending experts to chair the discussions. It also appoints *rapporteurs* for each proposal to be evaluated. All experts must look through all proposals. Depending on the wish of the panel members, after a certain period of time, e.g. half a day, the first *rapporteur* gives a report on one proposal. This is then discussed, and the *rapporteur's* task is to incorporate the result of the discussion into the report. After he has done so, the resulting document is again discussed, and finally accepted, through consensus. If single panel members disagree, they can do so by having a minority statement added to the report. Normally, this is not the case. The agreed and signed report is then given to the Commission representative.

### Workload

Workload is a decisive factor for the quality of the working results. The number and size of research proposals that the panels are expected to evaluate are probably at the upper limit of what reasonably can be managed. However, this would pre-suppose that the information needed for the evaluation was provided in a comprehensive and understandable manner. It has been stated before that this is normally not the case. Therefore, a lot of time is spent on identifying and collecting the information needed. That time then is lacking for the actual evaluation of that information.

### Factors to be considered by the panels

According to Commission documents, experts are requested to “identify the ethical issues at stake, assess if the proposer(s) is providing evidence that he/she/they are aware of the ethical issues and take(s) the appropriate measures to fulfil all ethical and/or legal requirements” (1).

The issues the panels are to look at comprise the information the researcher is supposed to give with regard to the animal experiments he plans to undertake and the other ethical issues:

- justification of the type and number of animals to be used;
- justification of how the principles of *reduction*, *refinement* and *replacement* are fulfilled;
- in the case of use of non-human primates: species specified, origin, modalities of importation, or breeding of animals, etc; and
- justification of the use or creation of transgenic animals (9).

The *rapporteurs* have to sum up in their reports the following points:

- objectives of the research and benefit for humans, animals or the environment (based on proposal and scientific evaluation);
- identification of ethical issues;
- evaluation of “human ethics”; and
- evaluation of “animal ethics” i.e. animal welfare aspects.

Clearly, the task of the panels is not restricted to merely identifying the relevant information, but to come up with conclusions, comments and recommendations. They must state whether the research complies with ethical principles, as laid down in Community legislation (and ethical principles beyond that legislation — see below) and/or “give suggestions for improvement” (1).

### Information available at the panels

With regard to particular research proposals, experts participating in an ethics panel receive from the Commission the proposal, the summary report from the scientific evaluation and eventually further information on the ethical aspects of the research given by the proposer that had been requested from the Commission.

With regard to information that is not directly linked to specific proposals, as mentioned before, the evaluation takes place in a meeting room in a Commission building in Brussels, and thus, there is hardly any access to external information. If specific questions come up at the meetings, the Commission staff is willing to help to retrieve the information, e.g. from the Internet. But this is, and is meant to be, rather an exceptional case. The Commission does provide information to the evaluators on a regular basis by making a number of more or less relevant documents available to each evaluator. The following documents were available at an ethics panel meeting in 2000.

Documents that are not particularly relevant with regard to animal use:

1. Background Note.
2. Extracts of Information Package.
3. “Work Programme”.
4. Extract of *Guide for Proposers (Part 1)*.
5. Convention on human rights and biomedicine of the Council of Europe.

6. Declaration of Helsinki.
7. UNESCO Declaration on Human Genome.

Documents that are relevant for animal welfare issues:

8. *Convention ETS123* of the Council of Europe for the protection of vertebrate animals used for experimental and other scientific purposes.
9. *Directive 86/609/EEC* on the protection of animals used for experimental and other scientific purposes.
10. Opinion of the European group on ethics on the “ethical aspects of genetic modifications of animals”.
11. Checklist for specific requirements on animal research applications, provided by the Animal Welfare Academy.
12. Publication *Ethical Scoring Systems* of the Canadian Council on Animal Care.
13. Ethical scheme proposed by the European Centre for the Validation of Alternative Methods (ECVAM; 10).

The high proportion of documents relating to animal welfare may reflect the efforts of the Commission staff to underline the importance of this aspect. Nevertheless, the question could be asked whether the provision of all of these documents helps to improve the quality of the evaluation. It has been mentioned before that the workload for the experts is over the limit. Therefore, the evaluators cannot be expected to be able to read through the background documents in addition to the research proposals they have to examine. Consequently, only those who know the contents of the documents can make proper use of them.

## Evaluation criteria

### *Animal welfare criteria*

A lack of expertise in animal welfare issues in the Commission’s ethics panels is reflected by a lack of animal welfare criteria applied in the evaluation. According to the personal experience of the author of this article, there is hardly ever a veterinarian on a panel. Therefore, for instance, questions of anaesthe-

sia cannot be properly addressed. The question whether an alternative would be available also cannot be properly answered because the knowledge needed for a competent decision in that regard is not there either.

However, once animal welfare criteria *are* applied, remarkably, they may go beyond existing legislation. For example, better housing and care standards than the minimum requirements as laid down in the Annex to EU *Directive 86/609/EEC* may be regarded as necessary by the panels.

### *Cost–benefit analysis*

One would expect that a cost–benefit analysis of the research would be in the centre of the evaluation process. But this is not the case. The reason for this is in the Commission’s evaluation system. The scientific quality of the research, i.e. the benefit, once stated by the scientific panel, cannot be really questioned by an ethics panel. Therefore, there is not much room to decide that, generally, it cannot be regarded ethical to use animals to reach the scientific objective. To doubt the relevance of (aspects of) a research proposal that has passed the scientific evaluation would mean to question the competence of the scientific panel.

## Outcome of an evaluation

Therefore, the outcome of an evaluation, at least in the field of animal experimentation, is more or less based on two criteria.

1. Is the quality and quantity of the information concerning the proposed animal research satisfactory?
2. Does the information given generally raise doubts about the ethical justification of the research?

There are two important aspects in this context. The first is that, even if it may appear to be a paradox, normally, the more information that is provided in a proposal, the higher the risk that a panel may identify particular problems. And the second aspect is that it is entirely up to the Commission to decide which consequences should be taken as a result of the outcome of the evaluation process.<sup>18</sup>

In general, there are three options with regard to the follow-up of the ethical review.

1. In case the ethics panels do not express any concerns about the ethical acceptability of the pro-

<sup>18</sup>“The Commission will take into account the comments made by the ethical review panel during the contract negotiation phase and before any contract is concluded” (8).

posed research, the Commission may take up the contract negotiation with the proposal author without any reservation concerning ethical aspects.

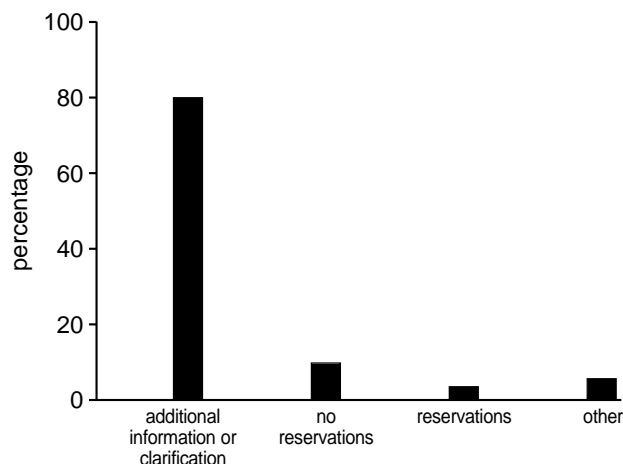
2. If the panels conclude that there is a need for further information or clarification, the Commission asks the proposal author to provide this information in the technical annex of the contract.
3. In case the panels have reservations, the Commission may invite the proposal author to meet representatives of the panel to be able to respond to these reservations. According to the Commission "funding of the project will not be granted before the panel has expressed its satisfaction" (1).

It is highly interesting to have a look at the statistics with regard to these options. The following numbers do not specifically refer to ethical aspects concerning animal experimentation, but to all types of ethical aspects. However, they are suitable to generally demonstrate the outcome of ethical evaluations: out of 143 proposals submitted to an ethical review from 1999 to 2001 (Figure 2), only 15 (10%) passed the review without any concerns by the panels. In 115 cases (80%) additional information or clarification was required. And in seven cases (5%), reservations were expressed by the panels (1).

These numbers confirm that a majority of proposals do not contain the necessary information to an extent and of a quality that would suffice to endorse them on ethical grounds. The fact that only few proposals led to other consequences than merely to ask for information or clarification on the other hand cannot be taken as a proof that only few proposals do not comply with the relevant ethical principles. They may also indicate that certain ethical aspects are not sufficiently considered in the evaluation, or they are not followed up in a satisfactory way.

To give a concrete example, in an evaluation the panel stated that the researcher had not sufficiently justified the type and number of animals to be used. There were no other negative comments concerning this proposal, so the consequence was not that the researcher had to come to a hearing with panel members. Neither is a second evaluation foreseen in such a case. That means, applying the Commission's above-mentioned principles for the follow-up of the evaluation, the proposal author had to specify the information in the technical annex. Whether this specification was sufficient, and whether it did not raise any doubts about the ethi-

**Figure 2: Outcome of ethical review of research proposals (1999–2001)**



Source: reference 1.

cal acceptability of the research was never subject to a review.

The concrete effect on the protection of animals of the ethical evaluations that have been undertaken in the past seems to be in the reduction of animal numbers and use of non-human primates in particular.<sup>19</sup> The Commission believes that there is also a rather psychological effect on the society's reflection over the use of animals in science and research that may lead to higher ethical standards.<sup>20</sup>

### Special aspects

Compared to the work of other types of ethical committees, experience has revealed some special characteristics in the work of the European Commission's ethics panels.

1. In the ethics panels meetings, there is usually an open and constructive atmosphere. Experts are willing to listen to each other, and even to learn from each other.
2. The Commission representatives, as the moderators of the meetings, do not attempt to influence the discussions or decision in one direction or the other.
3. Normally, at least some of the experts are not personally involved in the animal experimen-

<sup>19</sup>"The follow-up of the ethical reviews has in several cases led to reduction in the number of animals to be used in particular non-human primates which, in some cases, were replaced by studies in other animals" (11).

<sup>20</sup>"These measures are contributing to increase the awareness and to establish a dialogue at European level between scientists and experts in ethics and animal welfare issues, which may contribute to the process of consensus forming around an ethical conduct and a more responsible behaviour" (11).

tion issue — they are neither researchers nor animal welfarists.

## Outlook

Obviously, the current evaluation scheme cannot fulfil the expectation that EU-funded research always complies with state-of-the-art ethical standards for animal use in research. There is no simple answer to the question of what needs to be done to improve the ethical acceptability of EU-funded research. But there are clear opportunities for improvement of a variety of factors that have been shown to jeopardise the success of the Commission's initiatives toward the ethical use of its research grants.

### A better formal framework

Present EU legislation on animal experimentation is out of date in many aspects. For example, the manifold possibilities of genetic modification of animals could not be foreseen at the time when that legislation was drafted; new knowledge on the ethology of animals used in laboratories and ways to better comply with the resulting demands on housing and care has been gained since then. Current legislation also does not take into account many factors that play a role with regard to the *reduction, refinement and replacement* of animal experiments, and with regard to the requirements for a proper evaluation, authorisation, and/or licensing scheme. It, therefore, provides for an unsatisfactory basis for ethical considerations concerning research proposals. *Directive 86/609/EEC*, in particular, needs to be amended thoroughly, and as soon as possible. The amendment process has finally started, and it is to be hoped that it will lead to a considerable improvement of the current law.

At the same time when defining the bottom line for what should be regarded as legal within the EU, the Commission needs to define higher standards for the ethical basis of EU-funded research. Just as only the most excellent research, in scientific terms, should receive EU money, so should only the most ethical research. Clearly, there is a need to firmly define which ethical standards should apply for the framework programmes. This is not an easy task, but there are ways to accomplish it. A variety of issues exist where it is clear that there is no consensus in the EU's societies about their ethical acceptability. The use of non-human primates in research is one such example. The European Parliament has expressed its desire to stop experiments on non-human primates. Consequently, as long as such experiments are still legal, the Commission should at least refrain from supporting them financially.

## Better applications

The experts who have the task of evaluating ethical aspects of research do so on the basis of written proposals. The deficiencies of proposals with regard to ethical aspects have been identified above. To improve the quality of the research proposals in this respect, clearer and more stringent requirements are needed. For example, the use of internationally accepted pain and distress catalogues should be mandatory in describing animal experiments. At the present stage, forms to be filled in would probably make it easier for researchers to understand which information they are obliged to provide.

For large projects (project clusters), there should be a requirement to provide a comprehensive overview of all animal use within the individual projects.

The fulfillment of formal criteria concerning the description of the ethical aspects of the proposed research should be a mandatory prerequisite for a proposal to become subject to a review at all. For example, whether a researcher has provided the estimated number of animals to be used or not is not a question that needs to be answered by external experts. This can certainly be done by Commission staff, and if the information is not there, no panel should be asked to look at the proposal.

## Better panels/experts

To improve the level of expertise within the ethics panels with regard to animal research aspects, experts with a background in animal welfare issues in general, and Three Rs approaches in particular, and in ethical aspects of animal experimentation, need to be identified and encouraged to be involved in ethical evaluations; then, the number of experts on the panels that possess such a background needs to be significantly increased.

## Improved evaluation process

To improve the actual evaluation process, clearly, either more time for the evaluation of the present quantity of proposals must be provided or, for the presently foreseen amount of time, fewer proposals should be evaluated.

The evaluators require clearer guidance wherever possible, i.e. objective criteria on how to handle the information given in the proposals.

The scientific value of a proposed research must no longer be excluded from the ethical evaluation. On the contrary, it needs to be systematically considered. In particular, it should be clearly distinguished in between the overall value of a whole research project and the value of the animal experiments that are to be carried out to answer specific questions.

## Toward a satisfactory outcome

To provide for a more satisfactory result of the efforts undertaken to examine from an ethical point of view research proposals for the European Commission, clear criteria must be set up to describe the actions to be taken.

For example, when the panel concludes that a procedure is not carried out in the way which inflicts the minimum amount of suffering, e.g. by neglecting humane endpoints, there should be a clear way to proceed, e.g. by accepting a proposal only on the grounds that the appropriate methods will be used, or by rejecting the proposal and asking for an amended version in which the appropriate measures are planned, or possibly even by rejecting the proposal as a whole, because it has become clear that the proposal author either does not have the knowledge or resources to comply with agreed upon ethical principles or is not willing to give them sufficient consideration.

To guarantee that researchers follow through with the requirements that they have either acknowledged themselves, or that have been stipulated by the Commission, there must be some type of control. To that end, a continuous and retrospective ethical evaluation of the research undertaken is needed. In case of obvious non-compliance with the ethical standards, this should result in penalties up to cancellation of the contract. For example, when unforeseen circumstances are responsible for a drift in the cost-benefit ratio of the research, this requires a new overall ethical evaluation of the proposal. At the same time, this type of situation must be analysed, and conclusions must be drawn for future evaluations.

## More transparency

A review scheme that aims at assuring the ethical acceptability of EU-funded research must, by definition, aim at acceptance from all parties involved and from the public. Acceptance can only result from understanding, and the basis for understanding is transparency. The Commission has undertaken considerable efforts to make its ethical review process transparent. In particular, it has recently made most of the relevant information on that process publicly available on the Internet (1, 11). On the other hand, this is merely general information, whereas any specific information on ethical aspects of specific research projects remains undisclosed. The citizens of Europe have a right to be informed about the concrete ethical aspects of the research that is funded by their taxes. They should know animal species and numbers and levels of pain and distress in animals that are involved in that research. Any research conducted with support from the EU results in a report, and these reports

should contain that information. This may lead to a better and more widespread reflection on what can be regarded as ethically acceptable or what should be worthy of receiving money, from an ethical perspective.

The task to define that ethical framework cannot (and should not) be left to bioethicists or politicians. That definition can only be the result of a democratic opinion- and decision-making process. In humankind's history, the view of the acceptability of many practices has changed as a consequence of this process. With a view to animal experimentation, society must have a chance to redefine its values and ethics, and transparency in the field of animal experimentation is needed for that.

The suggestions given above for an improvement of the ethical evaluation scheme that the Commission has set up are merely meant as an impetus for a discussion. A retrospective analysis of the entire evaluation process is needed, and input from experts (bioethicists, animal welfare experts, and so on) will be needed to identify problems and to draw up possible solutions.

In the end, the European Commission, the European Parliament and the European Council would have the responsibility to transform the results of the above mentioned analysis into a formal framework that provides for a better basis to guarantee the acceptability of EU-funded research. This needs knowledge, motivation and the courage to make even painful decisions, if needed for the sake of a policy that is worthy of being called humane.

The alternative is unacceptable. The Commission has expressed the view that its ethical review process has a wider effect on the attitudes within the research community, on the political importance of the issue and on the future legislation of Member States and Associated States. It would be disastrous if the wider effect were that the ethical review is just seen as a formal step on a checklist that does not require adherence to the highest ethical standards possible. Many ethical review schemes that are in place all over the world have failed to do what the public expects from them. The Commission's ethical review process still has a chance to become a better example of a society's responsibility toward animals.

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