

**Technical Expert Working Group  
for the revision of Directive 86/609/EEC on the protection of animals  
used for experimental and other scientific purposes**

**Final report  
Sub-Group Cost-Benefit**

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# **Review of EU Directive 86/609/EEC Technical Expert Working Group Final Report from Cost-Benefit Sub-Group**

## **Introduction**

The TEWG (Technical Expert Working Group) Sub-Group tasked with addressing the question of the severity classification and cost-benefit analysis of Directive 86/609/EEC, began its discussions on 1 July 2003 and posted its first draft report on the Circa website. This final report summarises the opinions, and where consensus was reached, during subsequent discussions, carried out via the Circa website and by e-mail, involving members of the Cost-benefit Sub-Group and also other members of TEWG.

The discussions took place in the context of advice received from the European Commission that, in relation to the Directive, there was no specific competency for animal welfare at EU level. This competency was a matter for member states. The current Directive was based on a need for good functioning of the internal market and harmonisation of related practices across the EU. On this basis, the scope of the Directive could not extend to the use of animals in basic research or in education and training. It was noted, however, that national legislation generally applied to these areas as well as to the areas covered by the Directive. However, in the absence of advice to the contrary, the work of the Sub-Group Cost-benefit was carried out based on the competency advised by the EC.

In this report, 'Members' refers to members of the Sub-Group Cost-benefit of the TEWG.

## **4. SEVERITY CLASSIFICATION**

### **Definition of Severity Classification:**

This defines the upper limit of pain, suffering, distress or lasting harm that may be experienced by an individual animal during the course of a procedure. This limit will take into account the alleviation of pain, suffering, distress or lasting harm by the use of, for example, analgesia, anaesthesia and/or humane endpoints.

### **4.2.1 Minimum criteria for severity classification.**

#### ***What would be the optimum number of classes?***

The members agreed that the number of severity classes for animals used in procedures should be three.

### **Arguments**

Experience from the MS shows that three categories are the most practical approach.

We recognize that there is a high diversity in the different national approaches of severity classification (from no classification required up to 7 levels scale). The directive should ensure that minimum requirements are in place throughout the EU and leave to national authorities the responsibility to develop detailed modalities and definitions.

***How should the classes be defined to ensure a harmonised approach?***

**Definition of classes**

(Regarding technique, procedure, project, the group used the definitions agreed on by the rapporteurs, see below 4.2.2.)

The following classes apply to animals used in procedures.

**Class 1:** see remarks from the plenary presentation in Brussels on Nov 7 and proposals made to slightly reword the definition.

- Procedures, which may cause no more than momentary distress or pain
- Procedures, which are performed under terminal anaesthesia
- Procedures, which cause minor distress or pain of short duration

**Class 2:**

- Procedures, which cause moderate distress or pain or momentary distress or pain of greater severity

**Class 3:**

- Procedures, which cause enduring moderate distress or pain
- Procedures, which cause severe distress or pain that cannot for scientific reasons be alleviated

**Arguments:**

The group did not agree whether the classes should be named mild, moderate, severe or whether assignment of letters, e.g. A, B, C would be more appropriate.

Some member of the group felt that further considerations should be given to animals carrying harmful mutations and the genetical modified animals (we refer to scope, should the breeding of genetically modified be considered as a procedure).

This "moderately detailed" approach will avoid too wide discrepancies in classification of comparable procedures by the responsible scientists. As explained in the *Report of cost-benefit working group of the UK animal procedure committee* (see library), "a number of difficulties are inherent in the classification of severity of protocols [...] because different people have different understanding of, views on, and perceptions and interpretations of, the terms suffering, severity, mild, moderate, and substantial". Such differences, observed in the understanding of a single national law, should be taken into account in the application of a common system throughout 25 countries (or more in the future).

One member suggested that the definitions under Class 2 and Class 3 procedures should, as for Class 1 procedures, be phrased “may cause” instead of “cause”, just as the suggested definition of severity classification says “--- that may be experienced by an individual animal”. When the classification relates to the situation for the animal only after proper anaesthesia and/or analgesia, it would be dependant on an assurance for this situation to be at hand.

***What factors should be considered when assigning a severity class e.g. terminal/non terminal, use of anaesthesia?***

Criteria to be considered:

- Duration of distress or pain
- Intensity of distress or pain
- Frequency of interventions
- Deprivation of ethological needs (e.g. housing, temperature, social behaviour, food/water)
- Use of anaesthesia & analgesics

#### **4.2.2 Application of severity classification**

##### **Practical use of severity classification**

***Should each experiment/project be assigned to a severity class?***

##### **Background:**

##### **Definitions**

Definitions of terms that would be appropriate to include in Sub-Group reports should be as follows

- a. **Technique:** A technical act carried out on one or more animals for an experimental or other scientific purpose and which may cause that animal pain, suffering, distress or lasting harm, e.g. gavage, injection, laparotomy, withholding of food/water
- b. **Procedure:** A combination of one or more technical acts carried out on an animal for an experimental or other scientific purpose and which may cause that animal pain, suffering, distress or lasting harm
- c. **Project:** A coherent program of work aimed at meeting a defined scientific objective or objectives and involving a combination of one or more procedures

Severity classes are only relevant and practicable for procedures and not for projects

##### **Arguments:**

The reason for this are:

- that projects will include several procedures from different severity classes. Assigning a single class to projects would then necessitate the calculation of a mean or average

severity which is not relevant in terms of animal welfare. This is also a very strong suggestion from the report on cost-benefit working group of the APC (UK) saying that *"We conclude that overall severity bands are inadequate both for the purpose of cost-benefit assessment and providing public information about severity. On these grounds, we doubt the value of assigning overall severity bands for projects, and invite the Home Office to consider reviewing the utility and effectiveness of severity banding for assessing, monitoring and managing projects"*.

- at the time a project is launched, there maybe little specific information available on the details of the procedures that will be required to answer the questions addressed by the project. Research projects are continuously evolving based on the results of in-vitro, in-vivo and clinical investigations that justify and impact on the design of subsequent procedures.
- it has been proposed that severity assessment of procedures should initially be suggested by the researcher and this assessment should be evaluated and confirmed by the ethical review process, which would not be responsible for assessing projects .

***How should the level of severity be taken into account in the ethical evaluation and authorization procedure?***

The group felt that this question should be discussed with the authorization and ethical review group.

*Severity classification should be part of the ERP and not of the authorization procedure which should rather concentrate on the authorization of the institution, based on the information supplied about the facilities, the training of personal, the ERP in place, general husbandry procedures and the use of the best practices.*

*Experience in some countries has shown that in depth ERP and evaluation of individual experiments at the authorities level (rather than at the level of the local ethical committee) was not compatible with the resources available to the authorities in charge of animal welfare in many countries and would have a dramatic and unacceptable impact on the approval timing of protocols.*

*Therefore, as expressed during the July meeting of the group, severity classification should be*

- *part of the local ERP,*
- *within the responsibility of the researcher*
- *verified by the local care and use committee*

***What should be the requirements regarding re-use and severity classification?***

1. Animals that have been subject to severity Class 2 or 3 procedures should not be re-used.
2. Animals that have been subject to severity Class 1 could be re-used subject to ERP.

**Arguments:**

1. They should not be re-used in cases where the memory of distress or pain may potentially increase the perception of pain in subsequent procedures. (see article 10 of current directive)

**Comment:**

The potential re-use of animals may have important consequences on the total number of animals used. It seems important to avoid any complete ban on the re-use of animals.

During the discussion that took place on Nov 7, some participants also stressed the fact that in some cases, it may be needed to perform several procedures of level 2 class on the same animals. This is for example the case of animals that undergo surgery for placing telemetry devices before being used in several procedures comparing several compounds or several doses of a similar compound. The possibility to consider all these related technical acts as a single procedure has been proposed to solve this potential problem.

**Explanation.**

Re-use is normally used to describe an animal that has experienced a procedure from which it has fully recovered and returned to normal and is then re-used in an unrelated procedure where another naïve animal might as well have been used.

Surgically prepared animals that have other techniques applied to them after recovery are a single continuing procedure, (See Definitions 4,2,2)

Animals that are, for example, dosed with a succession of derivatives of a chemical compound and where the effects need to be compared to the effects of previous administrations, ie the animal is serving as its own control, then that is a single continuing procedure.

If the chemicals being used as in the example above were unrelated then that would constitute 're-use' and it would be usual to only re-use the animal once.

**Harmonization across the EU**

*How can a harmonised approach to severity classification be ensured throughout the EU to avoid transfer of experiments from one Member State to another?*

See 4.2.1 and 4.2.2

The group felt that the risk of transfer of experiments from one Member State to another because of lack of harmonization in severity classifications throughout the EU is minimal (if any).

**Comment:**

There is however a significant risk of transfer of research programs (and corresponding investments) outside the EU and, in a certain extend, such transfer already takes place when national legislations in European countries induce excessive burden of bureaucracy or impose unjustified constraints when compared to non European countries.

**Changes in the experiment and retrospective analysis**

*How to identify and record it if the severity in the actual experiment will be different than planned?*

The severity class attributed by the researcher to each procedure and endorsed by the local ERP should be communicated to people in charge of the daily care of the animals and any deviation from the expected severity class should be reported to the competent person within the institution (see art 5.d of the Directive) and the ERP.

The competent person within the institution should decide on appropriate corrective measures and record it. This should also be taken into account for subsequent protocols by both the researcher and the ethical review committee.

**Comment:**

National legislation may require that severity classes attributed to procedures including animals are communicated to the authorities, for example in addition to the yearly statistics on animal use. Some members strongly argued against the requirement, for each institution, to make this information publicly available since:

- the publication of figures from several hundreds of institutions will not help the public in making its own opinion and to identify major trends.
- as annual statistics, the communication to the public of sensitive information from individual institutions would, in many countries, raise strong confidentiality and security concerns that may encourage the transfer of some research programs and related investments to other countries
- provisions for the protection of confidentiality of sensitive information are included in the current Directive under art 13 (2)
- This level of details in the requirements should remain at the level of the Member States, to better reflect local cultural specificities.

*Should a retrospective analysis be carried out to verify actual level of severity? If so, should results be made publicly available?*

*How should this information be used for the benefit of future experiments?*

See previous question/answer

#### **4.2.3 Guidelines on severity classification**

*What kind of guidelines could be developed to identify the appropriate severity classification?*

Guidelines should be established that are workable and best on current best practice. The Commission should seek expert advice.

*What general guidelines could be identified to reduce severity e.g. application of humane end-points, the use of appropriate medication during and after the experiment, recognition of symptoms of pain and distress at an early stage?*

Some of the guidelines are already in the library.  
FELASA guidelines.

Suisse guidelines  
etc

**4.X Other identified issues**

## 5. COST BENEFIT ASSESSMENT (?)

The cost benefit assessment should weigh the benefit likely to accrue from a project against the likely adverse effects on the animals used.

There were differing views among Rapporteurs as to whether Cost-Benefit was the correct term or whether, for example, Harm-Benefit, Benefit-Harm, Benefit vs Harm or some other title was more appropriate.

Regardless of this, the following **definition** for cost benefit assessment was agreed:

A weighing of the likely adverse effects on the animal or animals concerned against the benefits likely to accrue as a result of the project submitted for authorisation.

### **Comment:**

One member argued that cost benefit assessment appears to be redundant with justification of the procedure and demonstration of implementation of the 3Rs.

In addition there is no evidence to date that cost benefit assessment, where it was introduced, proved any efficiency in terms of improving animal welfare or decreasing number of tests. In addition, it seriously calls into question fundamental research where direct benefit of a program is not always obvious. Therefore a detailed and well reasoned scientific justification and demonstration of 3Rs application, which are both part of the ethical review, should be preferred..

Some concerns were also expressed on the relevance and justification of cost / benefit analysis for **regulatory tests** where the process for cost / benefit assessment would not benefit to the welfare of animals but result in significant increase of bureaucracy.

### **5.1.1 Cost Benefit Analysis**

The group suggests that the term cost-benefit **assessment** should be used.

*Should there be a compulsory cost-benefit assessment of experiments?*

Yes.

*If so, should it apply to all experiments or only to specific ones depending on type, species and severity?*

All procedures involving the use of animals should be subject to a cost benefit analysis before, during and after the work.

*What should be the minimum requirements for a cost-benefit assessment?*

a) Prospective Cost Benefit Assessment.

The project proposal should include a critical evaluation of the need for and justification of using animals at all and the measures to be taken to minimize the suffering of the animals used. The proposal should also include a consideration of any alternative or non-sentient work that may negate or reduce the animal usage. It should give an assessment of the likely harms to the animals

and justify that they are acceptable using the basis of the minimum possible harms caused are consistent at least with the probable benefits that may accrue.

The prospective assessment should consider the overall objectives and scientific merit of the project and judge them worthwhile, achievable and realistic. The moral defense of the project is contestable depending on opinion. However, there should be a consensus by all involved with the project that its inception can be justified.

Once the cost benefit assessment has been conducted the proposal should be submitted for authorization at an appropriate level.

#### b) Interim Cost Benefit Assessment

- The severity class attributed by the researcher to each procedure and endorsed by the local ERP should be communicated to people in charge of the daily care of the animals, so that any deviation from the expected severity class could be reported to the competent person within the institution (see art 5.d of the Directive).
- Each animal procedure should be the subject of interim cost benefit assessment. Adverse effects should be observed and compared to those described in the project submission. Animal care technicians, the researcher and the veterinary surgeon should liaise in deciding if the degree of severity is consistent with that which is authorised.

Some members expressed their concerns about the validity of interim cost / benefit since, at that stage, the results, and expected benefits, from the procedure were not known and since potential deviations from the expected cost were already addressed in the section concerning the retrospective severity classification.

- If, after the end of a procedure, a retrospective assessment considers the degree of severity or the severity limit to have been breached an appropriate adjustment must be agreed before the project is allowed to continue.

See also 4.2 xx and authorisation

#### **Retrospective Cost Benefit Assessment of the project**

##### ***How to analyse and record the actual cost and benefit at the end of the project?***

At the end of the project, a report should be submitted to the ERP for evaluation against which was proposed originally. The retrospective assessment of the Cost Benefit of the procedures within the project will involve an assessment of the value of the data obtained and the 'balance' of harm to which the animals were subjected.

This proposal was not shared by all members. The reason for this was that such a cost benefit assessment at the project level was felt inappropriate and meaningless for reasons exposed earlier in this report and according to which, cost benefit should only be considered at the procedure level. This has also been stressed in the report on cost-benefit working group of the APC (UK)

saying that " we find implausible that careful and detailed cost-benefit assessment, of the kind required under the Act, can be carried out in the case of large licenses that cover a wide range of different kinds of study, united by a general theme; or which license certain tests that can be carried out in a variety of different circumstances."

One member commented that the suggested prospective and retrospective cost benefit assessments at the project level and interim cost benefit assessment at the procedure level would need careful phrasing, clarifying that the demands for assessment has two different levels.

(Comment: These values cannot be quantified and are very subjective. The values are not specifically assessed in most scientific publications which usually focus on the data procured by the work. However, the value of a retrospective assessment within an institute is to develop a body of experience in the management of animal experiments.).

***How should this information be used for the benefit of future experiments?***

This information should be used to inform future cost benefit assessments, prepare best practice guides and help to improve experimental design.

**5.2.2 Guidelines on cost-benefit assessment**

***What should be included in guidelines for cost-benefit analysis, and what specific factors should be considered during the assessment?***

The group agreed that guidelines on cost benefit assessment are needed and the Commission should seek expert advice for drafting such guidelines.

**5.X Other identified issues**

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**Composition of the Sub-Group Cost-Benefit:**

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<b>Marlies Halder (chair)</b>	<b>(ECVAM)</b>

The Members of the TEWG were expected to act as individuals and not as representatives of the national authority or non-governmental organisation that nominated them.

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