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Summary

Complementary to existing legislation, non-public research companies in France have been working together voluntarily within an organization known as Grice (Interprofessional Working Group on Ethics Committees for Laboratory Animals/Groupe de Réflexion Interprofessionnel sur les Comités d'Ethique appliquée à l'animal de laboratoire) with the objective of creating institutional ethics committees in an effort to promote animal welfare and good scientific procedures. Each company's commitment to the creation of these committees has been expressed by signing the Charter. Each ethics committee is composed of at least three members, including one who is not a scientist; a veterinarian is highly desirable. The committee examines all procedures and protocols involving animals and hands down a favourable or unfavourable opinion, or requests improvements, especially concerning animal well-being. Consensual approval of the protocol is an essential requirement before the purchase or allocation of animals. The committee examines every aspect of laboratory animal housing and care, and inspects all temporary or permanent animal housing facilities. Grice will continue its efforts in relation with public research organizations as well as with groups and in other countries whose objectives are in line with its own.

Keywords Laboratory animals; company research; protocol review; animal care and use; scientific quality; ethics committees

Within the framework of the EC directive 86/609/CEE (le Conseil des communautés européennes 1986) translated into national law, French legislation concerning the use of animals for research or for other scientific purposes (le Premier ministre 1987) has opted for the approval of establishments concerned and for the empowerment of research workers. In France, each research scientist must personally hold a licence to conduct experiments and is therefore legally responsible for carrying them out in accordance with the law (le ministre de l'Agriculture 1988). This licence to conduct experimental work is granted by the Bureau of Veterinary Services in each geographical department, subject to compliance with strict criteria concerning the field of experimentation and the training and competence of experimental workers. And yet, despite the nature of such regulatory authorizations, further consideration and harmonization might be needed for the

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practical application of the legal requirements imposed on the use of animals in research (Bonnod 1992). For this reason French company research organizations and research scientists have taken the lead in creating institutional ethics committees (Peyclit 1994).

Monitoring bodies of this type have proved effective in several EC member states (Verhoog 1989, Townsend & Morton 1995, Autissier 1997), as well as in Canada (Conseil canadien de protection des animaux 1993, Létourneau 1994, Demers 1999), in Australia (Brennan 1995, Anderson & Perry 1999) and in the US (Hamm *et al.* 1995, ILAR 1996b). These local committees ensure improved efficiency through direct contacts with professionals in animal experimentation.

The situation in France has been described recently (Milhaud 1996). Regional committees were created in Lyon or Toulouse, and a proposal to develop the national Inter-organisation Committee for Ethical Discussion and Control of Animal Experimentation for public research has not so far progressed. However discussions continue (Lachapelle & Bach 1999).

The inspection systems developed in France by the Ministry of Agriculture rely mainly on the Bureau of Veterinary Services. Their action is, however, frequently restricted to a consideration of the animals' environment and welfare (Eloit 1992). Internal ethics committees can ensure the exhaustive implementation of the three Rs (Reduction, Refinement and Replacement) (Russell & Burch 1959, Balls 1997).

The role of the ethics committee is thus to ascertain that the use of animals for research and other scientific purposes is conducted under strict ethical and legal conditions. It is with this goal in mind that ethics committees provide assistance and support to research scientists (Jennings 1994).

Grice

French companies in the private research sector have cooperated in an effort to promote the creation of institutional ethics committees, and to define the scope of their operations. Grice (Interprofessional Working Group on Ethics Committees for Laboratory Animals/Groupe de Réflexion Interprofessionnel sur les Comités d'Ethique appliquée à l'animal de laboratoire) was founded in 1990 as a working group of Gircor (Groupe Interprofessionnel de Réflexion et de Communication sur la Recherche) (Maurin-Blanchet 1998). Two years later, the Group drafted the following Charter.

Charter for ethics committees as applied to animal experimentation

(1) Each company signing this Charter acknowledges that the quality of research work requiring the use of laboratory animals is dependent on the well-being of those animals, and on the ethical conditions surrounding their use.

(2) Despite the fact that French legislation does not specifically require the creation of institutional ethics committees for animal experimentation, companies signing the Charter have agreed on the principle for several years.

(3) The Ethics Committee is an authorized body which hands down opinions in an independent manner. Its primary mission is to ascertain that laboratory animals are used only when necessary, and under the best possible conditions, and that their well-being and protection is assured with respect to the objectives of each company.

(4) The role of the Committee is as follows.

  (a) To ascertain that the use of laboratory animals is in compliance with national legislation.

  (b) To ascertain that conditions relating to the supply, housing, husbandry and care of animals are optimized both in terms of facilities and in terms of procedures.

  (c) To list, classify and examine all experimental protocols requiring the use of laboratory animals, and to issue an opinion approving or disapproving the protocol, or to propose modifications.

  (d) To promote the exchange of information and the training of staff in animal protection.

(e) To assist the company in replying to any question related to the use of laboratory animals.
(f) To evaluate all protocols and, when needed, the conditions under which subcontracted research programmes are conducted.

(5) Operation.
(a) Members of the committee must have access to all facilities involving the housing or use of laboratory animals.
(b) Members will have the necessary resources to accomplish their task.
(c) In the area of the Ethics Committee's operations, members are entirely free to express their opinions.
(d) All opinions and documents of the Committee are subject to internal confidentiality procedures specific to each company.

(6) Composition of the Committee:
(a) The Committee is to consist of at least three members, one of whom is not a scientist.
(b) Invited participants:
- the person requesting the approval for the study protocol or the experimental schedule;
- the person in charge of the study protocol or of the experimental schedule;
- one or more persons invited by the majority of the members.

In signing this Charter, each participating company commits to creating internal ethics committees complying with the principles described therein. To date, over 25 companies have signed the Charter.

Grice, as being established by private research, has no relationship with the regional committees or other public research committee. The success of Grice is due to member companies committing to common objectives and guidelines but remaining free to select the most appropriate structure. Nothing was imposed by Grice but the Charter which sets out the minimum requirements to organize an effective ethical committee.

Scope of the ethics committee

The Charter is the reference document, but the following recommendations, based on acquired experience, specify and expand the basic principles it contains.

The ethics committee examines every research protocol involving the use of living animals, as well as other aspects related to laboratory animals. Areas situated within the ethics committee's activity (Brugère *et al.* 1992b) are presented in the underlying sections. The considerations and decisions of the committee or research scientist will reflect state-of-the-art information available in the literature, or provided by experts as needed (Allen & Jensen 1996, de Greeve & de Leeuw 1997, Stafleu *et al.* 1999).

Justification of the protocol

The rationale and purpose of the protocol is examined. Availability of replacement methods and potential unnecessary duplication of experiments are reviewed (Nab *et al.* 1993, Balls 1994). In certain cases, preliminary research may be required, which must also have the committee's approval.

Selection of animal species

The most appropriate animal species will be selected for a given protocol (van der Gulden *et al.* 1993). Selection is based on scientific or regulatory grounds. Non-vertebrate animal species are not covered by the European Directive and Grice will have to make proposals on this point.

Number of animals

The number of animals is determined in such a manner as to guarantee the scientific and/or regulatory validity of the protocol. Using animals in numbers which are in excess of, or not sufficient for, the protocol's requirements is ethically unacceptable (Engeman & Shumake 1993). For a given protocol, the appropriate number of animals must be justified by scientific (internal or external), regulatory or statistical references (McCance 1989, Festing 1994).

Pain assessment (ILAR 1991, Brain et al. 1995)

The assessment of pain which may be inflicted through the implementation of a protocol is accomplished using 'yes/no' answer or graduated scales (Porter 1992). Pain-inducing protocols are subject to particularly strict examination (IASP 1980, LASA 1990) and the use of anaesthetics or analgesics must be routinely considered. Humane endpoints will be established.

Stress and discomfort (Brugère et al. 1992a, Townsend 1993)

Within a given protocol, those aspects causing stress or discomfort, e.g. isolation, instrumentation, or restraint (Mroczek 1992) will be examined. If such procedures are deemed to be required, their negative impact on animals must be minimized through the use of animal acclimatization and comforting (ILAR 1992).

Surgery

All surgical procedures are to be performed using anaesthesia in compliance with good professional practice (Flecknell 1996). The use of post-surgical analgesics must be routinely considered (Brown *et al.* 1993).

Euthanasia

The only euthanasia methods allowed are those specified in the report issued by the European Commission (Close *et al.* 1996, 1997).

Housing facilities (le Conseil des communautés européennes 1986, ILAR 1996a)

Housing conditions and facilities used for experimental animals must at the least comply with existing legislative requirements, or, in the absence of such legislation, must comply with professional standards. The ethics committee may be consulted over administrative questions concerning animal experimentation, (e.g. legal approval of the establishment), although it is not responsible for such matters. The committee ensures that all aspects of the protection of personnel against protocol-related biological risks are taken into consideration.

Training

Any training provided to research workers, laboratory technicians or animal technicians must be appropriate and in compliance with legal requirements and existing standards. The ethics committee strongly encourages the training of staff in technical, scientific and ethical issues.

Suppliers and shipping

The conditions under which the animals are bred and transported must be clearly stated and approved by responsible parties within the establishment. The committee must be kept informed.

Ethics committee members and relations with site management

An ethics committee must include at least three members. The actual number will vary with the size of the institution, and with the final objective of reflecting appropriate representation of activities performed. At least one of the members should be a non-biologist. Whilst it is recognized that some biologists have become highly competent in the fields of laboratory animal physiology and pathology, and that training is indicated (Nevalainen 1999), the presence of a veterinarian as a committee member is nevertheless highly recommended (Fioramonti 1996, Milhaud 1996). A veterinarian from outside the company can be consulted.

In accordance with needs expressed by members, the committee may invite individuals to contribute on specific issues. These visiting members will enhance the breadth of the committee's opinions. Such individuals may be researchers, scientists or experts. The participation of a person from outside the company who is experienced in social or moral issues furthermore guarantees that such issues are taken into consideration (Dresser 1999). Such participation is nevertheless left to the discretion of the site management and of its committee.

Inasmuch as the creation of the ethics committee is a decision originating from each of the companies rather than any legal obligation, the committee reports to the company management who has authorized the committee to issue opinions. The company management is also responsible for ensuring that the committee's opinions/recommendations are upheld. Finally, the company management approves the method by which the committee selects its members, and assures that all appropriate areas are represented.

The ethics committee's activities and operation

The committee's activities consist of meetings, inspections and the drafting of documents.

Committee meetings serve mainly for the examination of protocols and for the exchange of information. The frequency of the meetings may vary as needed. Attendance may involve all or some members, depending on the subjects under review and the relevant nature of each member's participation.

The committee examines, lists and classifies all procedures and protocols involving the use of animals. It can approve the documents or reject them, or may request changes usually relating to animal welfare. Protocol approval is therefore a prerequisite for the purchase or allocation of animals. Approved protocols are periodically reviewed and/or revised: the committee's decisions may change just as knowledge and technology may change. Sub-contracted protocols are also reviewed, except where the sub-contractor otherwise reports to a committee that it is operating in compliance with these recommendations. No general overview of the impact of the review on the protocols has been made until now, but preliminary data coming from some companies indicate that most protocols submitted need complementary information following their first review, and that 10–30% of the protocols need modifications for approval. Some protocols cannot be approved.

Committee meetings give members the opportunity to exchange information on legislation, recommendations, publications, conferences and recent technology, as well as on internal affairs. Whenever necessary, the committee forwards information or questions to Grice.

Minutes are drafted following each meeting, whether plenary or whether it involves only some of its members. These minutes are then distributed to either a general or a restricted audience, depending on their contents and specific provisions for the company. General circulation may facilitate the committee's activities within the company concerned.

Inspection is essential for all facilities and housing used for animals in a permanent or a temporary manner. Regular inspections constitute a core activity of the committee. Not only are these inspections useful in assessing the animals' physical environment, but they also represent an opportunity to meet the technical staff and the research scientists. Such meetings may provide an opportunity to discuss protocols and/or procedures.

The ethics committee drafts an annual activity report describing the committee's objectives and achievements. This document should be distributed as extensively as possible.

Any person within the establishment may submit a general or specific issue to the committee to obtain an assessment. It then decides on a case-by-case basis whether or not to pursue the matter.

The committee may also engage in other activities, such as the drafting of internal documents, the distribution of external documents within the company, or the organization of presentations, training sessions or information briefings for newly employed staff. Finally, the committee may assist the company in its relations with internal committees such as the Chsct (the hygiene, safety and health committee/Comité hygiéne, sécurité et conditions de travail), or with persons from outside the establishment, e.g. veterinary inspectors or other visitors.

Conclusions and prospects

Over recent years, non-public research companies in France using laboratory animals have voluntarily created institutional ethics committees. Decisions within Grice and acquired experience have created a set of common operational guidelines for these committees. These guidelines have been presented in the form of the recommendations in this document.

Grice will soon draft a set of recommendations intended to offer ethics committees a standardized and well documented means to evaluate protocols. These recommendations will draw upon efforts which have already been completed, or which are underway, in other countries. For this purpose, Grice will engage and expand relations with groups and structures sharing similar aims in other countries.

Grice will also seek to exchange information with public research institutions in order to encourage the creation of ethics committees within these entities.

Finally, Grice will establish communications with organizations having an interest in its aims, for the purpose of providing information on its activities.

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References

Allen T, Jensen d'A (1996) IACUCs and AWIC: the search for alternatives. *The Johns Hopkins–Center for Alternatives to Animal Testing* **13**, 1–6

Anderson WP, Perry MA (1999) Australian animal ethics committees: we have come a long way. In: *Cambridge Quarterly of Healthcare Ethics*. Cambridge: Cambridge University Press, pp 80–6

Autissier C (1997) Systèmes de réglementation mis en place en Europe pour s'acquitter des responsabilités éthiques. *Ressource* **21**, 6–7

Balls M (1994) Replacement of animal procedures: alternatives in research, education and testing. *Laboratory Animals* **28**, 193–211

Balls M (1997) The three Rs concept of alternatives to animal experimentation. In: *Animal Alternatives, Welfare and Ethics* (van Zutphen LFM, Balls M, eds). Amsterdam: Elsevier, pp 27–41

Bonnod J (1992) Ethique en expérimentation animale. *Sciences et Techniques de l'Animal de Laboratoire* **17**, 201–5

Brain P, Palanza P, Parmigiani S (1995) Evaluating pain and distress in laboratory animals. *Scandinavian Journal of Laboratory Animal Sciences* **22**, 18–20

Brennan A (1995) Ethics, welfare and money. In: *Animals in Science Conference. Perspective on their Use, Care and Welfare. Proceedings* (Johnston NE, ed). Monash Australia's International University, pp 1–15

Brown MJ, Pearson PT, Tomson FN (1993) Guidelines for animal surgery in research and teaching. *American Journal of Veterinary Research* **54**, 1544–59

Brugère H, Laurent J, le Bars D, Mahouy G, Milhaud C, Schmitt S, Wintergerst J (1992a) Douleur, souffrance, stress, peur, angoisse et anxiété: définitions et commentaires. In: *Expérimentation Animale: Mode d'emploi*. Paris: Inserm ed, pp 15–22

Brugère H, Laurent J, le Bars D, Mahouy G, Milhaud C, Schmitt S, Wintergerst J (1992b) Pratique de l'expérimentation animale. Mise en oeuvre d'un protocole expérimental: lignes directrices. In: *Expérimentation Animale: Mode d'emploi*. Paris: Inserm ed, pp 23–57

Close B, Banister K, Baumans V, Bernoth E-M, Bromage N, Bunyan J, Erhardt W, Flecknell P, Gregory N, Hackbarth H, Morton D, Warwick C (1996) Recommendation for euthanasia of experimental animals: Part 1. *Laboratory Animals* **30**, 293–316

Close B, Banister K, Baumans V, Bernoth E-M, Bromage N, Bunyan J, Erhardt W, Flecknell P, Gregory N, Hackbarth H, Morton D, Warwick C (1997) Recommendation for euthanasia of experimental animals: Part 2. *Laboratory Animals* **31**, 1–32

Conseil canadien de protection des animaux (1993) La responsabilité du soin et de l'utilisation des animaux d'expérimentation. In: *Manuel sur le Soin et l'Utilisation des Animaux d'Expérimentation*, 2nd edn. (Olfert ED, Cross BM, McWilliam AA, eds). Ottawa: Bradda Printing Services Inc, pp 1–15

de Greeve P, de Leeuw W (1997) Developments in alternatives and animal use in Europe. In: *Animal Alternatives, Welfare and Ethics* (van Zutphen LFN, Balls M, eds). Amsterdam: Elsevier, pp 127–36

Demers G (1999) La politique de protection animale au Canada. *Sciences et Techniques de l'Animal de Laboratoire* **24**, 39–42

Dresser R (1999) Community representatives and nonscientists on the Iacuc: what difference should it make? *ILAR Journal* **40**, 29–33

Eloit M (1992) Principes de la réglementation française en matière d'expérimentation animale. *Sciences et Techniques de l'Animal de Laboratoire* **17**, 151–4

Engeman RM, Shumake SA (1993) Animal welfare and the statistical consultant. *American Statistician* **47**, 229–33

Festing MFW (1994) Reduction of animal use: experimental design and quality of experiments. *Laboratory Animals* **28**, 212–21

Fioramonti J (1996) IACUCs & me: a community vet's story. *The Johns Hopkins–Center for Alternatives to Animal Testing* **13**, 86

Flecknell P, eds (1996) *Laboratory Animal Anaesthesia*, 2nd edn. London: Academic Press

Hamm TE Jr, Dell RB, van Sluyters RC (1995) Laboratory animal care policies and regulations: United States. *ILAR Journal* **37**, 75–8

Institute of Laboratory Animal Resources (ILAR) committee (1991) Recognition and alleviation of pain and distress in laboratory animals. *ILAR News* **33**, 71–4

Institute of Laboratory Animal Resources (ILAR) committee, eds (1992) *Recognition and Alleviation of Pain and Distress in Laboratory Animals*. Washington: National Academy Press

Institute of Laboratory Animal Resources (ILAR) committee (1996a) Animal environment, housing and management. In: *Guide for the Care and Use of Laboratory Animals*. Washington: National Academy Press, pp 21–55

Institute of Laboratory Animal Resources (ILAR) committee (1996b) Institutional policies and responsibilities. In: *Guide for the Care and Use of Laboratory Animals*. Washington: National Academy Press, pp 8–11

International Association for the Study of Pain Committee (1980) Ethical standards for investigations of experimental pain in animals. *Pain* **9**, 141–3

Jennings M, eds (1994) *Ethics Committees for Laboratory Animals: a Basis for their Composition and Function*. London: Royal Society for the Prevention of Cruelty to Animals

Laboratory Animal Science Association working party (1990) The assessment and control of the severity of scientific procedures on laboratory animals. *Laboratory Animals* **24**, 97–130

Lachapelle F, Bach A (1999) Faut-il instaurer des comités d'éthique sur l'expérimentation animale? *INSERM actualités* **166**, 20–2

Le conseil des communautés européennes (1986) Directive 86/609/CEE du Conseil du 24 Novembre 1986 concernant le rapprochement des dispositions législatives, réglementaires et administratives des Etats membres relatives à la protection des animaux utilisés à des fins expérimentales ou à d'autres fins scientifiques. *Journal officiel des Communautés européennes L* **358**, 1–6

Le conseil des communautés européennes (1986) Annexe II à la directive 86/609/CEE du Conseil du 24 Novembre 1986 concernant le rapprochement des dispositions législatives, réglementaires et administratives des Etats membres relatives à la protection des animaux utilisés à des fins expérimentales ou à d'autres fins scientifiques. *Journal officiel des Communautés européennes L* **358**, 7–28

Le premier ministre de la république française (1987) Décret n°87–848 du 19 Octobre 1987 pris pour l'application de l'article 454 du code pénal et du troisième alinéa de l'article 276 du code rural et relatif aux expériences pratiquées sur les animaux. *Journal officiel de la République française* **243**, 12245–8

Le ministre de l'agriculture (1988) Arrêté du 19 avril 1988 fixant les conditions d'attribution de l'autorisation de pratiquer des expériences sur les animaux. *Journal officiel de la République française* **99**, 5608

Létourneau L, eds (1994) *L'expérimentation Animale: l'Homme, l'éthique et la loi*. Montréal: Thémis

Maurin-Blanchet H (1998) Le (Gircor) Groupe Interprofessionnel de Réflexion et de Communication sur la Recherche. *Sciences et Techniques de l'Animal de Laboratoire* **23**, 151–60

McCance I (1989) The number of animals. *News in Physiological Science* **4**, 172–6

Milhaud C (1996) Protection de l'animal de laboratoire; rôle des vétérinaires dans les comités d'éthique. *Bulletin de la Société des Vétérinaires Praticiens de France* **80**, 315–27

Mroczek NS (1992) Recognizing animal suffering and pain. *Laboratory Animals* **21**, 27–31

Nab J, Balls M, Hendriksen CFM (1993) Alternatives to animal experimentation. In: *Principles of Laboratory Animal Science* (van Zutphen LFM, Baumans V, Beynen AC, eds). Amsterdam: Elsevier, pp 319–33

Nevalainen T, Berge E, Gallix P, Jilge B, Melloni E, Thomann P, Waynforth B, van Zutphen LFM (1999) FELASA guidelines for education of specialists in laboratory animal science (Category D). *Laboratory Animals* **33**, 1–15

Peyclit I (1994) Structure et objectifs des comités d'éthique. In: Ethique et expérimentation animale: application à un centre de recherche pharmacologique. *Thèse pour le diplôme d'Etat de Docteur en Pharmacie*. Limoges pp 36–7

Porter DG (1992) Ethical scores for animal experiments. *Nature* **356**, 101–2

Russell WMS, Burch RL, eds (1959) *The Principles of Humane Experimental Technique*. London: Methuen

Stafleu FR, Tramper R, Vorstenbosch J, Joles JA (1999) The ethical acceptability of animal experiments : a proposal for a system to support decision-making. *Laboratory Animals* **33**, 295–303

Townsend P (1993) Control of pain and distress in small laboratory animals. *Animal Technology* **44**, 215–25

Townsend P, Morton DB (1995) Laboratory animal care policies and regulations: United Kingdom. *ILAR Journal* **37**, 68–74

van der Gulden WJI, Beynen AC, Hau J (1993) Animal models. In: *Principles of Laboratory Animal Science* (van Zutphen LFM, Baumans V, Beynen AC, eds). Amsterdam: Elsevier, pp 189–96

Verhoog H (1989) Ethical committees In: *Animal Experimentation: Legislation and Education* (van Zutphen LFM, Rozemond H, Beynen AC, eds). Utrecht: Veterinary Public Health Inspectorate, pp 129–38