UKCCCR Guidelines for the welfare of animals in experimental neoplasia

Prepared for the UKCCCR by an ad hoc committee comprising:

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Background and scope

Animals with local or disseminated tumours are likely to experience pain and/or distress, thus justifying special care and attention from both licensees and others involved in their welfare. Associated techniques including surgical preparation, irradiation, and drug administration may increase the severity of an experimental procedure. Recognizing this, the United Kingdom Coordinating Committee on Cancer Research (UKCCCR1), representing the main cancer charities and the MRC, has prepared the following guidelines for research workers using animals in experimental neoplasia. Particular emphasis is focused on the prediction and recognition of adverse effects and the implementation of humane end points. The majority of work in this area utilises small laboratory animals, particularly rodents. Consequently we have drawn largely on available expertise with these species. However, the general principles are applicable to all species of animal.

While we recognize and encourage the development of alternative research techniques which do not involve animals, we consider that there are many questions which can be answered only by the study of tumours growing in vivo. The general welfare of laboratory animals and the performance of regulated procedures upon them are both covered by the Animals (Scientific Procedures) Act (1986) effective from 1 January 1987. Under this Act all scientific procedures on living vertebrates which may have the effect of causing pain, suffering, distress or lasting harm are controlled by the Home Office and require specific authority through Personal and Project Licences. Recommendations for the housing and care of laboratory animals are specified in the Royal Society/UFAW Guidelines (Part 1, 1987). In addition, the following references are recommended for advice on general animal husbandry and experimental techniques: Gay (1965), Fowler (1978), Tuffery (1987) and the Institute of Animal Technology (in press).

We welcome the new Act and the Royal Society/

1 Member Organisations of UKCCCR: Cancer Research Campaign, Imperial Cancer Research Fund, Institute of Cancer Research, Leukaemia Research Fund, Marie Curie Foundation, Medical Research Council, Tenovus Cancer Fund.

Observers: Department of Health and Social Security, Ludwig Institute for Cancer Research, Scottish Home and Health Department.
UFAW Guidelines, and look forward to the publication of further guidelines from expert sources. We envisage that the present guidelines will be of general value to workers carrying out experiments which involve the growth of tumours in experimental animals, whether these arise spontaneously, are produced by transplantation (including passage and hybridomas), or are induced by carcinogenic agents or genetic manipulation. They may be especially helpful in the completion of Project Licence Applications, in particular section 19b (v and vi) which requires that applicants list the possible adverse effects and their likely incidence as well as the proposed methods of controlling severity, e.g. the use of analgesia, regional or local anaesthesia and sedation, and the implementation of humane end points.

It is an important feature of the present guidelines that the procedures practised upon animals in cancer research, and particularly the humane end points used, should be subject to a continuous process of refinement. The guidelines will therefore be modified and updated as appropriate. The guidelines are not mandatory. The term 'should' is used to encourage attainment of desirable standards; the term 'must' is used only where legal obligations apply.

The Recommendations are divided into two parts. The General Recommendations are applicable to all regulated procedures. The Specific Recommendations are more directly targeted to the particular problems of experimental neoplasia. It is important to emphasize that procedural guidelines, especially with respect to implementation of humane end points, must be tailored to the precise nature of each individual experimental neoplasia model. To illustrate this, the Appendix gives some examples of criteria for particular tumour systems.

**Recommendations**

**General recommendations**

1. The following recommendations are based on the premise that for each study those involved in the procedures will weigh the likely adverse effects on the animals used against the benefits likely to accrue from the work. The potential benefits of cancer research are clear. Nevertheless, the feasibility of using alternative methods not involving live animals should be considered. *In vitro* cell lines may be appropriate in many instances.

2. Where animals must be used, the degree of pain and distress must be minimised by judicious use of anaesthetics and analgesics, the refinement of experimental techniques, and the early implementation of humane end points. Licensees must know the severity band for each regulated procedure (i.e. mild, moderate, substantial or unclassified). The severity band will have been arrived at by agreement between the applicant and the Home Office and takes into consideration details of the procedure itself, the nature and incidence of any likely adverse effects and any practical measures which will be used to minimise severity. The severity condition of Personal and Project Licences requires a Personal Licensee to notify the Project Licence holder if one or more severity bands may have been or are likely to be exceeded. The Project Licence holder must notify the Home Office Inspectorate of this at the earliest possible opportunity. In addition, there is an inviolable termination condition in every Personal Licence, which requires the Personal Licensee to ensure the immediate killing (by an approved painless method) of any animal in severe pain or severe distress which cannot be alleviated.

3. Where certain procedures cause particular concern, these must be noted specifically in the Project Licence application. A more detailed justification and definition of severity limits will be needed. Such procedures may be subject to additional conditions in the Personal Licence to control numbers of animals and/or severity. In addition, the Home Office may require particular reports on them.

4. It is important that pilot experiments should be undertaken on small numbers of animals before new procedures are carried out on a larger scale. The pilot experiments should identify particular problems, define the time scale of critical events, and help to refine the appropriate end point. In all