Assessing the welfare of genetically altered mice

D J Wells (Chair)1, L C Playle (Secretary)2, W E J Enser3, P A Flecknell4, M A Gardiner5, J Holland6, B R Howard7, R Hubrecht8, K R Humphreys9, I J Jackson10, N Lane11, M Maconochie12, G Mason13, D B Morton14, R Raymond15, V Robinson2, J A Smith16 and N Watt17

1Department of Cellular and Molecular Neuroscience, Imperial College, Faculty of Medicine, UK; 2National Centre for the Replacement, Refinement and Reduction of Animals in Research, UK; 3Harlan UK Ltd, UK; 4Comparative Biology Centre, University of Newcastle, UK; 5MRC Mary Lyon Centre, UK; 6MRC National Institute for Medical Research, UK; 7Medical School, University of Sheffield, UK; 8Universities Federation for Animal Welfare, UK; 9GlaxoSmithKline, UK; 10MRC Human Genetics Unit, UK; 11Royal Society for the Prevention of Cruelty to Animals, UK; 12Department of Biology and Environmental Science, University of Sussex, UK; 13University of Guelph, Canada; 14Medical School, University of Birmingham, UK; 15Cancer Research UK, UK; 16Boyd Group, UK; 17Home Office, Dundee, UK

Summary

In 2003, under the auspices of the main UK funders of biological and biomedical research, a working group was established with a remit to review potential welfare issues for genetically altered (GA) mice, to summarize current practice, and to recommend contemporary best practice for welfare assessments. The working group has produced a report which makes practical recommendations for GA mouse welfare assessment and dissemination of welfare information between establishments using a ‘mouse passport’. The report can be found at www.nc3rs.org.uk/GAmice and www.lal.org.uk/gaa and includes templates for the recommended welfare assessment scheme and the mouse passport. An overview is provided below.

Keywords Mouse; genetic alteration; genetic modification; welfare assessment; passport

The use of genetically altered (GA) animals, particularly mice, in scientific procedures is increasing [Home Office Statistics of Scientific Procedures on Living Animals Great Britain 2002]. Estimates of the potential impact of genetic alteration on mouse welfare vary [Thon et al. 2002, Buehr et al. 2003]. This may be due, in part, to lack of collation and/or reporting of relevant information, other than the annual reports to the Home Office which record total numbers of mice, but do not collect specific information on phenotype and welfare. To capture this information nationally would require a standardized approach. Methods for assessing and recording GA mouse welfare differ in UK establishments and therefore there would be merit in defining a welfare assessment scheme, which would enable identification of mice with poor welfare and better benchmarking of numbers of animals that have compromised welfare due to genetic alteration. This principle was recognized by the APC in its Report on Biotechnology (2001) which recommended that a graded approach to the welfare assessment of GM animals should be

Correspondence to: L C Playle, NC3Rs, 20 Park Crescent, London W1B 1AL, UK. Email: laura.playle@nc3rs.org.uk

Accepted 17 August 2005 © Laboratory Animals Ltd. Laboratory Animals (2006) 40, 111–114
adopted, and which instigated the establishment of the GA mouse welfare assessment working group.

GA mouse welfare assessment working group

The working group was established in 2003 and membership covered a broad range of expertise including mouse geneticists, animal technicians, veterinary surgeons and animal welfare and behaviour experts. The working group has produced a report which outlines practical indicators of GA mouse welfare. The working group also recognized, however, that these may be subjective and that there is a need for increased research to support the development of objective indicators of pain, suffering, distress and lasting harm. The working group did not consider the generation of GA mice, which has been considered in detail elsewhere (Robinson et al. 2003). The full report covers an introduction to the use of GA mice; a review of the potential welfare issues; the value and general characteristics of welfare assessment; current practices, recommendations for welfare assessment including practicalities, responsibilities and dissemination; and future directions.

The working group concluded that being GA does not necessarily affect the welfare of an animal; indeed many GA mice do not show adverse effects. Genetic alteration does, however, have the potential to compromise animal health and welfare by causing or predisposing the animal to pain, suffering, distress or lasting harm and the key issue is to be able to rapidly identify such animals (Costa 1997, Dennis 2002).

The working group considered how welfare could be assessed within the constraints of a laboratory environment (e.g. resources, staff time, disturbance to the mice) and its recommendations are based on the experience of the members and on published data. In addition to setting out a welfare assessment scheme for GA mice, the report also describes a ‘passport’ system for use when GA mice are transferred nationally and internationally between establishments.

The recommendations for welfare assessment outline general principles and provide a framework which can be built upon and modified to suit local requirements. The welfare assessments are intended to be carried out at various time points in the animals’ life – neonate, weaning and subsequently for the period that the adults are normally maintained for that particular line, and the assessments are tailored in this respect. Welfare assessment should be carried out in newly bred and maintained lines of GA mice and in GA lines newly introduced into establishments. The information derived from the assessment is intended to form the basis of a ‘welfare profile’ (i.e. a subset of key, specific welfare indicators) and ‘passport’ for each GA line.

At the neonatal stage, the number of pups should be recorded and observed for appearance and activity (Lloyd et al. 2000). At weaning and during adulthood, it is recommended that a series of non-invasive assessment criteria be used to assess welfare. This includes recording numbers and assessment of general appearance and clinical signs. Templates for assessment-recording documents are provided within the full report.

The implementation of a ‘mouse passport’ system when transferring mice between establishments is also recommended – a template along with guidelines for completion are contained within the full report. Using the passport will facilitate the transfer of husbandry, care and welfare information to receiving establishments and will thus improve access to information and will inform animal care staff of any requirements for specialist care.

Members of the working group recognize that implementation of the recommendations may not necessarily represent a significant change for many UK facilities. Nevertheless, in some establishments applying the principles set out in the report would result in an improved and more structured approach to welfare assessment. Although experience or anecdote may suggest that the majority of GA mice show little or no welfare problems, or can be
managed in such a way as to prevent/minimize suffering, implementation of the welfare assessments and the objective recording system set out in this report will provide more definitive evidence of any ‘costs’ to the animals.

Implementation of the report’s recommendations clearly requires buy-in from all involved in the use and care of GA mice and it is intended that the ethical review process will play a key role in promulgating the recommendations.

Summary of recommendations

**Recommendation 1**

From a scientific, ethical and legal perspective establishments should have a mechanism in place to identify any GA mice that show adverse effects.

**Recommendation 2**

Structured welfare assessments should be carried out for (i) newly bred and maintained lines of GA mice, (ii) GA lines that are newly introduced into the establishment.

**Recommendation 3**

Welfare assessment of new lines of GA mice should be carried out in the neonate (where appropriate), at weaning and subsequently for the period that adults are normally maintained for that particular line. For adult mice the most appropriate time to carry out the assessment is at cage cleaning. Welfare assessment should complement the daily observations.

**Recommendation 4**

The welfare assessment should include a range of non-invasive indicators. In the neonate – skin colour, activity and presence of the milk spot; and, at weaning and in the adult – appearance, size, coat condition, posture, gait, activity levels, interaction with the environment and clinical signs. The welfare assessments should be carried out using a check sheet as a prompt or ‘aide memoire’.

**Recommendation 5**

At each assessment a record should be maintained of (i) the number of mice observed and (ii) any mice identified as having compromised welfare. For any GA mice that are identified as having a welfare concern, the particular indicators that lead to this concern should be recorded. Examples of forms that could be used for these purposes are provided in the full report (www.nc3rs.org.uk/GAmice, www.lal.org.uk/gaa). These examples are for guidance and are not intended to replace similar documents or systems already in place.

**Recommendation 6**

Information obtained as part of the assessment should be used to create a ‘welfare profile’, specific to the particular GA line, that can be used to identify mice with welfare concerns (this will be a subset of the indicators in the aide memoire plus any additional indicators). The welfare profile should be available in the same room as the mice. All records should be maintained centrally within the facility.

**Recommendation 7**

All staff required to carry out welfare assessments should receive appropriate training and this should be regularly reviewed.

**Recommendation 8**

Every establishment should have in place, a system with defined responsibilities to ensure that the relevant people are informed of any welfare issue and are able to take appropriate actions to protect the welfare of the animals concerned. Reporting mechanisms should be regularly reviewed to ensure that everyone is aware of the system, how it works and what their roles and responsibilities are.

**Recommendation 9**

Information pertaining to husbandry, welfare issues, breeding recommendations
and expected phenotype should be disseminated when GA mice are transferred between establishments. This should take the form of a ‘mouse passport’ and should be a physical record that passes directly to the animal care staff in the receiving establishment. A passport template is given in the full report [www.nc3rs.org.uk/GAmice, www.lal.org.uk/gaa].

**Recommendation 10**

The recommendations laid out in this report are intended to be minimally resource intensive, however, there are likely to be some resource implications for the establishment. It is recommended that establishments consider resources, particularly staff levels, to enable welfare assessments to be carried out without adverse implications on day-to-day animal care and this may require additional investment.

**Recommendation 11**

It is recommended that the ethical review process plays a key role in promulgating the recommendations outlined in this report.

**Recommendation 12**

This report provides a basis for welfare assessment of all GA mice. However, there is a clear need for further research to determine which easily assessable parameters provide the most useful information.

**References**


