

The **APC**
Animal Procedures Committee

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Meg Hillier MP
Parliamentary Under Secretary of State
Home Office
2 Marsham Street
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From the Chairman
Ms Sara Nathan

Date 8 November 2007

Dear Meg,

RESPONSE ON THE OPERATION OF THE ANIMALS (SCIENTIFIC PROCEDURES) ACT 1986 – Consideration for the discharge of GA animals from Animal (Scientific Procedures) Act.

In December 2006 the former Parliamentary Under Secretary of State wrote to the Animal Procedures Committee asking for its advice in relation to better regulation, specifically the discharge of GA animals from Animal (Scientific Procedures) Act.

The request was for the Committee's thoughts on whether, without risking or compromising animal welfare, or damaging public confidence, the current discharge criteria of the Animals (Scientific Procedures) Act 1986 should be revised.

Annexed to this letter I have included a copy of the Committee's report for which I would like to thank the GA Criteria Working Group members, chaired by Professor Keith Kendrick for preparing and the representatives of the Home Office Inspectorate for their advice. The Group also received valuable input from Mr Paul Logan of the Health and Safety Executive.

The Committee would like to point out that consideration for changes in the discharge criteria of GA animals from Animals (Scientific Procedures) Act 1986 is an extremely far reaching topic and if implemented, represent significant changes to current policy. Because of the short deadline for presenting its conclusions the Committee raised but did not have sufficient time to discuss two issues that result from making changes to current practice these are outlined in Section 4 of the attached paper

The report, sets out four options for consideration if a revision of the current discharge criteria for GA animals under the Animals (Scientific Procedures) Act 1986 were to be implemented. These are listed below in bold, with supplementary comments in italics.

- (1) Keep the current rules and modify them to remove any ambiguity by stating that all GA animals must remain under the auspices of the Animals (Scientific Procedures) Act 1986.**

This was viewed by the sub-committee as being the 'no release' option;

removing the possibility of any flexibility within the interpretation of the Animals (Scientific Procedures) Act 1986. As a secondary impact, this option reduces any driver for developing an effective GA animal welfare assessment screen.

- (2) Keep the current rules but recommend that a review of the situation be conducted after an acceptable welfare screening protocol has been validated.**

This option allows for flexibility in the future, such that new developments in welfare assessment could be incorporated into the implementation of the Act. However, it would rely on industry or academia/industry collaboration taking the lead in developing an acceptable welfare assessment screen.

- (3) Adopt (2) but make an immediate exception for reporter and inducible GM construct lines subject to a pilot study of GA welfare screening to confirm absence of harmful phenotypes.**

This was considered to be the most favourable proposition, as lines carrying reporter gene sequences, or constructs that can only be used for GM following exposure to other “trigger” factors, are likely to present relatively low risk with regard to the likelihood of adverse phenotypes. This option also includes a driver to develop a welfare screen, as this is commensurate with the release of GA animals. It also has a potential 3Rs benefit in that it could lead to more efficient utilisation of such lines in future.

- (4) Adopt (3) but allow all GA animals to be released from the Act, while a standardised welfare screen is developed in parallel.**

The Sub-committee considered that this option would be difficult to control and would not be appropriate in the absence of properly evaluated and accepted welfare screens.

The majority view of the Working Group was that any welfare screen would need to set the type, scale and duration of quantitative welfare measurements at a practical level for scientific establishments. It was envisaged that the responsibility for post release monitoring of animals would lie with the holding establishment rather than the Animal (Scientific Procedures) Inspectorate.

The precise details of an acceptable screen were considered outside the remit of this initial exercise and the development of such an assessment system would require further consultation with experts and professional bodies.

It should also be noted that, with respect to bureaucracy, it would be necessary to test stakeholder opinion regarding the acceptability of developing a welfare assessment screen in addition to specialist phenotype screens. The Group were also mindful that most establishments already carry out animal health monitoring which is likely to involve some welfare assessment. What is recommended here is that a further, validated post release process is developed.

However, the establishment of an effective pre- and post-release assessment scheme could ultimately lead to broader significant benefits for both animal welfare and science, not just GA animal monitoring.

Yours sincerely

Sara Nathan

**Consideration for the discharge of GA
animals from Animal (Scientific
Procedures) Act 1986.**

Consideration under Better Regulation and the Home
Office Simplification Plan.

October 2007

Members of Working Group

Professor Keith Kendrick (Chair)
Dr Michael Festing (APC)
Dr Peter Hunt (APC)
Dr Penny Hawkins (APC)
Dr Ken Simpson (APC)
Mr Paul Logan (Health & Safety Executive/DEFRA)
Professor Nic Wells (Imperial College London)
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Note: For the purposes of this document, the Working Group has used the term Genetically Altered (GA) as distinct from Genetically Modified (GM). The meaning of GA is defined as that used by the Home Office, Animal in Scientific Procedures Division.

A genetically altered animal is defined as:- an animal in which the heritable DNA has been intentionally altered, or which carries a genetic mutation recognised as harmful, or the progeny of such an animal.

This definition includes

- Animals produced by genetic modification [as defined in the Genetically Modified Organisms (Contained Use) Regulations 2000].
- Animals produced by induced mutagenesis
- Animals created by nuclear transfer procedures
- Animals created by the use of certain selective breeding strategies
- Harmful mutant lines arising from spontaneous mutations

It excludes animals with changes that are not heritable, such as gene therapy or DNA immunisation.

Please see point 1.11 for an explanation of the possible implications regarding the interpretation of this distinction.

1. Preliminary Discussions of 4th May and 26th June 2007

1.1. It is currently possible to discharge GA animals from the Animal (Scientific Procedures) Act 1986 if there are full health records for two generations including records of the full life span over one generation, showing no adverse effects. The basis for this requirement is that some adverse effects may arise in the second generation but not in the first¹. However, this level of evidence is perceived to be excessive by some since in the majority of cases animals from GA lines are not normally maintained beyond 6-12 months of age.

1.2. If GA animals were found to suffer after removal from the Animal (Scientific Procedures) Act 1986, some mechanism would have to be in place to ensure that the GA line in question came back under its control.

1.3. It is generally accepted as anomalous that GA animal lines lacking a specific gene through a spontaneous (normal) mutation may be outside of the Animal (Scientific Procedures) Act 1986 if no welfare problems are detected, whereas lines where the same gene had been deliberately manipulated would fall within it.

Proposal for change.

1.4. The Minister has asked for the Committee's advice on whether the current discharge criteria should be revised in the light of the current state of knowledge on welfare assessments and phenotyping methods, in order to ensure that animals are not placed within the controls of the Animal (Scientific Procedures) Act 1986 if they are not likely to suffer, but without weakening the provisions for the welfare of protected animals.

1.5. To maintain welfare standards (as distinct from health standards) it was agreed that before a GA animal could be discharged from the Animal (Scientific Procedures) Act 1986 there would need to be a structured, formal welfare assessment (or other form of post release monitoring) carried out to provide sufficient objective evidence that, despite genetic alteration, such animals did not have adverse phenotypes that could cause physical or psychological suffering.

Points to consider in relation to changing existing regulation.

1.6. Experimentally produced GA animals (primarily rodents and fish) are major contributors to the total number of animals reported annually as having procedures carried out on them under the Animal (Scientific Procedures) Act 1986. Other species currently listed in the annual statistics as genetically modified or with a harmful genetic defect are rabbits, sheep, domestic fowl and amphibians. However, it was felt that any changes to regulations should be limited to rodents, amphibians and fish in the first instance.

1.7. Breeding of any GA lines can only be carried out under a project license by trained personnel holding personal licences, or with appropriate delegated authority.

1.8. Spontaneously occurring mutants do not automatically come under the Act (except when kept for scientific purposes) even though they are subject to the same "suffering and severity" issues as those that are experimentally induced.

¹ Broom DM (1997) Assessing the welfare of transgenic animals. In Zutphen LFM & van der Meer M (eds) *Welfare Aspects of Transgenic Animals*, Springer, pp. 58-67

1.9. There is always some uncertainty about the level and nature of adverse effects that might occur following a deliberate genetic manipulation. There is therefore no obvious case for the creation of a GA line to fall outside of the Animal (Scientific Procedures) Act 1986 as it is difficult to be certain that no adverse effects will occur. However, it is generally accepted that a large number of GA lines, once established, show normal general behaviour and no apparent suffering that can be attributed to the genetic alteration.

1.10. GA animals are generally kept in controlled environments. If released from the Animal (Scientific Procedures) Act 1986 some GA lines might ultimately be housed in more conventional environments where their physiology could be affected in unpredictable ways. GA animals released from the Act would therefore still have to be monitored to determine whether being kept under different environmental conditions did result in them experiencing pain, suffering, distress or lasting harm. Alternatively, they may have to be released on condition that the same environmental conditions are maintained. Strategies to rapidly detect and alleviate suffering would be required, as is normal procedure required by the Animal (Scientific Procedures) Act 1986. There would also need to be a robust means of tracking the fate of “ex-Act” animals following release.

1.11. Notwithstanding the point above, there is one issue the Working Group were not in a position to consider:- would it be permitted to keep some GA animals released from the Animal (Scientific Procedures) Act 1986 outside of secure, regulated environments? This is because the GM Act (Genetically Modified Organisms (Contained Use) Regulations 2000: Defra) requires only GM animals to be contained within a secure environment unless given a consented release order. A small number of GA lines might not be covered by the GM Act so this will have to be clarified before any GA line is considered for release from the Animal (Scientific Procedures) Act 1986.

1.12. However, under the conditions issued with Certificates of Designation, any GA animal having been subjected to a completed series of regulated procedures shall continue to be kept at a designated establishment under the supervision of a veterinary surgeon. If an animal were to meet specific criteria that might enable discharge from the Animals (Scientific Procedures) Act 1986 it would thus still remain at a designated establishment unless a named veterinary surgeon issued certification that it would not suffer if it ceased to be kept at a designated establishment. It is the Working Group's opinion that veterinary certification for such release would not be issued, particularly if GA animals were involved.

1.13. The group did generally agree that certain lines of animals that have biomarker inserts (for example *luciferase* gene systems or Cre-recombinase lines) are unlikely to suffer as a consequence of being GM animals. Thus, such animals are potentially suitable candidates for possible discharge from the Animal (Scientific Procedures) Act 1986. However, the actual numbers of animals affected might be quite small.

1.14. It was considered that applications would only be made if the period of observations required to be carried out on a GA line to apply for its release from the Animal (Scientific Procedures) Act 1986 was reduced. In general it was thought that a more realistic period of longevity (currently two generations with one full life span) would be the maximum expected lifespan of animals from a GA line for scientific purposes (i.e. 6 to 12 months). An exception would obviously be where age-related phenotypes were expected or animals were to be kept for longer periods.

1.15. Finally, to allay public concerns in connection with GA animals, it would be a

useful precaution to emphasise that (i) full health and welfare records would be kept to monitor animals and ensure that they were not suffering any adverse effects, in the same way as required under the Act; and (ii) release from the Animals (Scientific Procedures) Act 1986 does not mean release from captivity and would not enter any food chain.

2. Welfare Assessment of GA Animals

The Working Group agreed that any decision on the feasibility of releasing GA animals from the Animals (Scientific Procedures) Act 1986 will critically depend upon the ability to assess their welfare effectively, both before and after release.

One of the Group's members reviewed the scientific literature on current developments in welfare assessment of GA animals. Some suggestions from that review are set out below and further information is given in the Appendix Section 7.

- The approach recommended by researchers addressing this issue is to use welfare "score sheets" to assess GA animal welfare and to detect whether adverse phenotypes are present.
- This should be carried out at various life stages, taking into account the fact that some adverse effects do not become apparent until adulthood or towards the end of an animal's life.
- One research group (Mertens and Rüllicke) has produced a fully evaluated assessment protocol, but work is ongoing by others and there is no evidence of an agreed method that is in common use.
- It takes time to assess the welfare of GA animals properly; resource issues (e.g. with respect to staffing levels) have been identified when trialling assessment schemes.

3. Considerations of the Working Group 4th September 2007

Summary of the Meeting:

3.1. Discussion of information gathered on GA 'Welfare' screening.

The Group agreed that currently there is no formally accepted welfare screening methodology that could be applied to any GA line under consideration for discharge from the Animals (Scientific Procedures) Act 1986.

Dr Hawkins contacted a variety of EU colleagues and contacts and found that a COST Paper is being drafted on a related matter, and that pre-weaning assessment methodologies are also in development.

Following the deliberations of the previous working group meetings it was clear that until a formal welfare assessment of GA animals could be determined, the Working Group did not feel that it would be able to endorse a proposal to discharge such animals from the Animals (Scientific Procedures) Act 1986.

3.2. Proposed advantages and disadvantages of changing the criteria for the release of GA Animals from the controls of the Animals (Scientific Procedures) Act 1986.

The Group felt that it would be useful to lay out the advantages and disadvantages by relating them to; (i) the Three Rs, (ii) science (note that this refers to the advantages and disadvantages *for scientists*, and does not refer to scientific validity) and (iii) reducing bureaucracy.

3.3. What advantages would result from releasing GA animals from the Animals (Scientific Procedures) Act 1986.

Three Rs:

3.3a. Releasing GA animals from the Act would require adequate welfare assessment, which would encourage and promote the use of comprehensive welfare screens. This would reduce the potential for suffering, as adverse effects would be detected and alleviated more effectively. Such a system could also help promote more widespread improvements in welfare assessment and the uptake of more objective monitoring schemes.

3.3b. Some lines could potentially be bred and supplied more efficiently through commercial breeders, since under the proposed changes, licences would not be required for breeding lines released from the Act.

Science:

3.3c. A comprehensive assessment screen would have to be used to establish that welfare is not compromised, which would potentially help counter the apparent public perception that all GM animals experience suffering.

3.3d. Releasing GA animals from the Animals (Scientific Procedures) Act 1986 would provide more logical consistency in a system where, at present, GA animal lines lacking a specific gene through a spontaneous (normal) mutation may be outside of the Act, whereas lines where the same gene had been deliberately manipulated would fall within it (irrespective of whether any harmful phenotype is reported or not).

Bureaucracy:

3.3e. It would reduce time taken in bureaucracy, in particular the paperwork involved in animal movement forms for specific GA animals.

3.3f. It would reduce the risk of technical infringements, for example where people may breed GA lines without realising that both project and personal licence cover is required.

3.4 What disadvantages would result from releasing GA animals from the Animals (Scientific Procedures) Act 1986

Three Rs:

3.4a. There may be concerns that the welfare monitoring of GA lines could be less stringent once they are outside the Animals (Scientific Procedures) Act 1986. There is also no indication as to what mechanisms would be in place to ensure that such lines would be brought back under the Act if adverse effects became apparent.

3.4b. There are currently no fully validated welfare assessment protocols, that have been endorsed by professional bodies, that could form the basis of an effective "welfare" screen for GA (or even non-GA) lines.

3.4c. Release from the Act could result in GA animals undergoing changes in diet or

environmental conditions that might subsequently reveal a negative impact on health and welfare.

Science:

3.4d. Under the current Animals (Scientific Procedures) Act 1986 any form of biosampling for the specific purpose of genotyping (i.e. not solely carried out for individual identification) is a regulated procedure. The vast majority of GM animals need to be genotyped, so even if a line was released from the Animals (Scientific Procedures) Act 1986 there would not be a large reduction in the number of reported procedures. (NB this would clearly not be the case were the wording of the current Act to be altered to permit tissue taken for identification to be used for other purposes)

3.4e. Technically, releasing GA animals from the Animals (Scientific Procedures) Act 1986 would result in an under reporting of the number of animals used for scientific procedures. This could be interpreted negatively by the public and lead to perceptions that numbers are being artificially reduced for political purposes, or that there has been a reduction in openness and transparency relating to animal use. There may also be concerns that GA animals could end up being housed outside of designated establishments (for example entering the food chain or being released into the wild).

3.4f. No assessment protocol could be completely effective, so there would be occasions where GA lines would have to be brought back under the Animals (Scientific Procedures) Act 1986. Such cases might result in adverse publicity and reduced public confidence in the validity of the assessment and release protocol.

3.4g. Even if welfare assessment protocols were to be agreed upon, they might prove too onerous for many organisations to contemplate using them.

Bureaucracy:

3.4h. Once released from the Animals (Scientific Procedures) Act 1986, GA animal handling would be controlled under the Defra; Genetically Modified Organisms (Deliberate Release) Regulations 2002. Nevertheless, it was questioned whether there was sufficient overlap between the two legislative processes (See discussion point 1.11 – only GM animals would be covered, not all GA).

3.4i In contrast to point 3.3f, the Group could foresee a potential increase in the incidence of accidental infringements, without welfare implications, caused by misclassification of animals. Though such technicalities could be classed as an administrative failure, this issue is important since the point of this Better Regulation exercise is to reduce such problems for establishments.

3.5 Additional considerations regarding GA lines carrying reporter genes or region-specific or inducible constructs as distinct from other GA lines.

The sub-Committee considered whether GA lines created for the purpose of visualising genes, or as part of the process for the control of spatial and temporal aspects of genetic modification, should be considered as distinct from other GA lines. These would include: (1) reporter constructs (e.g. luciferase, lac-z, green fluorescent protein etc.), (2) constructs that can only be used to delete or over-express genes when in combination (through breeding) with other constructs (e.g. Cre-Lox) or (3) lines with inducible constructs that allow a specific genetic modification to occur at any point in time following the administration of a chemical agent (e.g. tetracycline or

tamoxifen. The reasoning behind this is that that such specific lines should, by definition, exhibit no harmful phenotype and could only do so following their exposure to a particular 'trigger' factor (e.g. when a particular chemical is administered to the animals or when they are bred together with another GA line).

It was recognised that the activation of any "trigger factors" for scientific purposes would obviously bring such animals under the Animals (Scientific Procedures) Act 1986 but it was felt that there would be very few instances where researchers might wish to remove GM lines with inducible constructs from the Animals (Scientific Procedures) Act 1986.

In general it was concluded that releasing the above types of animals from the Act, in conjunction with appropriate welfare assessment and monitoring protocols and other relevant safeguards, could provide a useful "test case" for helping to validate the process and perhaps lead to the consideration of applications for releasing other types of GA lines in the future.

3.6 Working Group Proposals.

The sub-committee concluded that there were four options that it could suggest in relation to the Minister's request for advice regarding revision of the current discharge criteria for GA animals under the Animals (Scientific Procedures) Act 1986. These are listed below in bold, with supplementary comments in italics.

- (1) Keep the current rules and modify them to remove any ambiguity by stating that all GA animals must remain under the auspices of the Animals (Scientific Procedures) Act 1986.**

This was viewed by the sub-committee as being the 'no release' option; removing the possibility of any flexibility within the interpretation of the Animals (Scientific Procedures) Act 1986. As a secondary impact, this option reduces any driver for developing an effective GA animal welfare assessment screen.

- (2) Keep the current rules but recommend that a review of the situation be conducted after an acceptable welfare screening protocol has been validated.**

This option allows for flexibility in the future, such that new developments in welfare assessment could be incorporated into the implementation of the Act. However, it would rely on industry or academia/industry collaboration taking the lead in developing an acceptable welfare assessment screen.

- (3) Adopt (2) but make an immediate exception for reporter and inducible GM construct lines subject to a pilot study of GA welfare screening to confirm absence of harmful phenotypes.**

This was considered to be the most favourable proposition, as lines carrying reporter gene sequences, or constructs that can only be used for GM following exposure to other "trigger" factors, are likely to present relatively low risk with regard to the likelihood of adverse phenotypes. This option also includes a driver to develop a welfare screen, as this is commensurate with the release of GA animals. It also has a potential 3Rs benefit in that it could lead to more efficient utilisation of such lines in

future.

(4) Adopt (3) but allow all GA animals to be released from the Act, while a standardised welfare screen is developed in parallel.

The Sub-committee considered that this option would be difficult to control and would not be appropriate in the absence of properly evaluated and accepted welfare screens.

The majority view of the Working Group was that any welfare screen would need to set the type, scale and duration of quantitative welfare measurements at a practical level for scientific establishments. It was envisaged that the responsibility for post release monitoring of animals would lie with the holding establishment rather than the Animals (Scientific Procedures) Inspectorate.

The precise details of an acceptable screen were considered outside the remit of this initial exercise and the development of such an assessment system would require further consultation with experts and professional bodies.

It should also be noted that, with respect to bureaucracy, it would be necessary to test stakeholder opinion regarding the acceptability of developing a welfare assessment screen in addition to specialist phenotype screens. The Group were also mindful that most establishments already carry out animal health monitoring which is likely to involve some welfare assessment. What is recommended here is that a further, validated post release process is developed.

However, the establishment of an effective pre- and post-release assessment scheme could ultimately lead to broader significant benefits for both animal welfare and science, not just GA animal monitoring.

4. Animal Procedures Committee discussion 10th October 2007.

The Working Group presented their proposals and supporting information to the full Committee for their consideration. The Committee endorsed the Working Group's conclusions. However, in the subsequent discussion Committee members raised a series of issues, listed below, for which there has been insufficient time to provide further opinion.

- At the Animals (Scientific Procedures) Act 1986 conception it is believed that legislators took a precautionary approach to providing guidance on the possibility of releasing animals from the controls of the Act, largely because of a lack scientific evaluation of the harmful consequences and likelihoods from such an action. The Committee would have discussed if the precautionary approach assumption is still valid in light of GA technological advances and current welfare knowledge.
- Given the suggestion to develop definitive welfare assessment for GA animal release and the prediction that this may increase beaurocracy, the Committee would have also wished to explore how further welfare assessment might affect the current approaches involving veterinary (professional) judgement and evaluate the differences and similarities between the two approaches.

To conclude the Committee would ask that this report be viewed as a preliminary paper; consideration for the discharge of GA animals from Animals (Scientific Procedures) Act 1986 is an extremely far reaching topic. The Committee is aware that proposals presented in this report, if implemented, represent significant changes to current policy.

5. Appendix: Supplementary information on Welfare Assessment

Introduction

Most of the welfare assessment schemes have been set out and/or evaluated by (i) Mertens and Rüllicke, (ii) van der Meer et al., (iii) Jegstrup et al. and (iv) the GA Mouse Welfare Assessment Working Group. Professor Nicol is also examining behaviour as an indicator of welfare status in an ongoing project funded by the NC3Rs.

Mertens & Rüllicke

Mertens & Rüllicke (1999) selected parameters from the literature and designed score sheets for (i) birth and first 24 hours; (ii) days 2-10; (iii) day 11 – weaning; (iv) weeks 4 to 12; (v) weeks 7 – 12, including first gestation/litter; and (vi) 13th week onwards. They describe a pilot study that found the score sheets to be feasible and recommend 10 complete life histories per genotype (5 of each sex) for basic characterisation and welfare assessment. The score sheets were available online but are no longer easy to find (hard copies are available).

More detail is given in Mertens & Rüllicke (2000) which says that founders and individuals from the F1, F2 and F3 generations should be assessed. The authors state that the number of individuals required depends on a number of factors and suggest, as a rule of thumb, a minimum of 10 animals per genotype: wild type, hemi- or heterozygous and homozygous (5 of each sex) born in either F1 or F2 generation, i.e. 30 mice.

The most recent paper by Mertens and Rüllicke (2007) does not set out any new schemes but is a summary of their project to date. The authors state that “the first few generations of newly created mutant strains (founders, F1 and F2) need to be characterised with respect to their phenotype using health and welfare assessment guidelines” to ensure that wellbeing is unaffected². Claudia Mertens believes that full lifespan data is required.

van der Meer et al.

van der Meer et al. (1999) sets out a series of behavioural and morphological tests for neonatal transgenic mice, scored according to four levels of response; 0 (behaviour or response absent), 1 (signs of primitive response), 2 (clear but not yet mature response) or 3 (mature and full response in all aspects of execution such as coordination or strength). This is combined with data on life span, survival rate and *post mortem* pathology etc.

van der Meer et al. (2001) develops the scoring system further with a limited number of sensitive, easy to determine and non-invasive parameters (selected from the previous studies). There are three score sheets, two for the pre-weaning period (day 0 - day 6 and day 10/day 14) and one for the weaning and post-weaning period. The paper describes a trial of the sheets, in which it was found that monitoring on days 0 to 6 took < 5 min per litter of 4 –6 pups; days 10 and 14 took 5 – 10 min per litter; after weaning 15 – 20 min was required per litter. The authors conclude that score sheets are feasible provided that time and funding are sufficient and technicians are well-instructed. Ways of reducing monitoring time are suggested, e.g. binding sheets

² Mertens M & Rüllicke T (2007) Welfare assessment and phenotype characterisation of transgenic mice. *ALTEX* **24**: 46-48

into a log book.

Jegstrup et al.

Jegstrup et al. (2003) suggests four goals for a GA welfare assessment protocol:

- reveal any special needs or problems with a transgenic strain;
- cover the informational needs of the purchaser/user of the strain for handling, housing and breeding;
- refine the transgenic animal model by recommending relevant humane endpoints;
- prevent the duplication of animal models already developed.

The authors state that the existing welfare evaluations in the literature cover different aspects and none of them fulfil all four of the goals that they set out³. They suggest that a way forward would be to combine current protocols and test the result on strains with different welfare problems, selecting the most useful parameters and putting these together into a new welfare assessment procedure. They planned to continue their work in this area and, according to the authors, some papers are almost ready for publication.

GA Mouse Welfare Assessment Working Group

The report of the GA Mouse Welfare Assessment Working Group (2006) calls for a standardised approach to welfare assessment and outlines a framework that aims to achieve this. It also states that basic welfare checks carried out by technicians are likely to identify “only the more gross/obvious abnormalities” and recommends that more formal, structured welfare assessments should be carried out for (i) newly bred and maintained GA lines and (ii) GA lines newly introduced into the establishment. This should be done in neonates, at weaning and then for the period for which adults are normally maintained for each line.

Another notable point from the Working Group’s report is that, in the members’ experience, information relating to the animals’ welfare and care is frequently omitted when GA mice are transferred between research establishments (hence the requirement for a mouse passport). This suggests that there is also a risk that relevant information could be omitted if GA lines are discharged from the Act – unless changes are made to the current transfer paperwork.

³ They cite Morton & Griffiths (1985), Lloyd & Wolfensohn (1999), Costa (1997), van der Meer et al. (2001a and b), Mertens & Rüllicke (1999), Rogers et al. (1999) and Irwin (1968).

Publications addressing welfare assessment of GA animals

- GA Mouse Welfare Assessment Working Group (2006) *Assessing the Welfare of Genetically Altered Mice*. www.nc3rs.org.uk
- Jegstrup I, Thon R, Hansen AK & Ritskes Hoitinga M (2003) Characterization of transgenic mice – a comparison of protocols for welfare evaluation and phenotype characterization of mice with a suggestion on a future certificate of instruction. *Laboratory Animals* **37**: 1-9
- Mertens C & Rüllicke T (1999) Score sheets for the monitoring of transgenic mice. *Animal Welfare* **8**: 433-438
- Mertens C & Rüllicke T (2000) Phenotype characterization and welfare assessment of transgenic rodents (mice). *JAAWS* **3**: 127-139
- van der Meer M, Costa P, Baumans V, Olivier B & van Zutphen B (1999) Welfare assessment of transgenic animals: Behavioural responses and morphological development of newborn mice. *ATLA* **27**: 857-868.
- van der Meer M, Rolls A, Baumans V, Olivier B & van Zutphen LFM (2001) Use of score sheets for welfare assessment of transgenic mice. *Laboratory Animals* **35**: 379-389

Background to Better Regulation

Following recent reviews, including the Cabinet Office review of regulation in the pharmaceutical sector, the Davidson Review and the PWC administrative burdens project, the aim of the ASPD better regulation programme is to simplify current regulatory requirements and administrative processes under the 1986 Act and reduce compliance costs whilst maintaining animal welfare standards. As part of this we will also benchmark current best practice and evaluate specific proposals, including some put forward by stakeholders. We are not considering proposals that would require changes to the legislation, or other Parliamentary time, to deliver.

The project will be overseen and managed within the framework for implementation of the Home Office Simplification Plan, and will actively involve operational level practitioners from both industry and academia; licence holders and named persons; and (to further ensure that the protection of animals is not compromised) those with a special interest in animal welfare.

2. The criteria for the discharge of genetically modified animals from the controls of the 1986 Act

The 1986 Act makes provision for the protection of animals used for experimental and other scientific purposes and subjected to regulated procedures which may cause pain, suffering distress or lasting harm. We take the view that genetically modified animals should be assumed to be potentially more prone to pain, suffering, distress or lasting harm (“harm”), as a result of the genetic alteration, than the background strain from which they are derived. As a result we regulate their production, breeding and use⁴.

Nevertheless, we have always accepted that there will be some lines of genetically modified animals that are not predisposed to these harms, and have made administrative provision for the discharge of such lines of protected animals (at least for breeding purposes) from project licences. To date no such lines have been discharged from the controls of the Act and some stakeholders have commented recently that the burden of proof required to release a strain from the controls of the Act seems to be set so high as to prevent anyone from trying.

In the circumstances, the Minister would welcome the Committee’s advice on whether the current discharge criteria should be revised in the light of the current state of knowledge on welfare assessments and phenotyping methods, in order to remove any unnecessary obstacles currently preventing strains being discharged from the controls of the Act without weakening the provisions for the welfare of protected animals.

⁴ See “Guidance on Genetically Altered Animals and the Animals (Scientific Procedures) Act 1986”